RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

Vol. 74 MARCH 1960 No. 3

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GENERAL INFORMATION

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As a convenience to contributors to RADIOLOGY who are unable to supply prints for their manuscripts, the Editor can arrange for intermediate prints from roentgenograms.

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Number and Distribution of Roentgenologic Examinations for 100,000 People[1]

REYNOLD F. BROWN, M.D.,[2] JOHN HESLEP, Ph.D.[3] and WILLIAM EADS, M.D.[4]

THE USE OF ionizing radiation in medicine has reached such proportions that the resulting exposure to man requires re-evaluation. The gonadal dose, particularly, needs scrutiny, since the induction of deleterious mutations is the most important effect produced by the amounts of radiation under investigation. The world literature can be reviewed in the United Nations Report (3).

An accurate estimate of the gonadal or absorbed dose from diagnostic roentgenology is difficult. The estimate for the United States from all medical uses as given in the Laughlin and Pullman report of 1956 (2) is:

"The thirty year effective gonad dose per person for both x-ray diagnostic examinations and radiation therapy treatments thus is estimated to be at least 2 ± 1 roentgens and is more probably about 5 ± 3 roentgens."

Later, in this same report, a figure of 4.0 r is given as the probable gonad dose resulting from diagnostic radiologic examinations.

Estimates with such wide limits illustrate the difficulty of arriving at a precise figure. The figure of 4.5 r has been widely quoted as representing the dose per person from medical uses, and rarely are the limits of accuracy designated. To produce reliable estimates of the dose contributed by diagnostic radiology, the following information is required:

1. The number and distribution by age and sex of the diagnostic examinations in the population.
2. A knowledge of the mechanical and electrical characteristics of the radiologic equipment and their effect on dose.
3. A knowledge of the technics and their contribution to gonadal exposure.
4. The variability in gonadal exposure due to the size and weight of the patient.

This report investigates only the first of these requirements. The "probable average exposure per examination" resulting from evaluation of numbers 2, 3, and 4 will be those of the Laughlin and Pullman study of 1956.

Webster and Merrill (1) showed the decreases in the gonadal dose that were obtained by assuming different "average exposures," such as prevailed in their installation. Such assumptions resulted in a calculated total dose at the lower level of the estimates of Laughlin and Pullman.

[1] Presented at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15-20, 1959. This study was made possible by a grant from the U. S. Public Health Service through the California State Department of Public Health.

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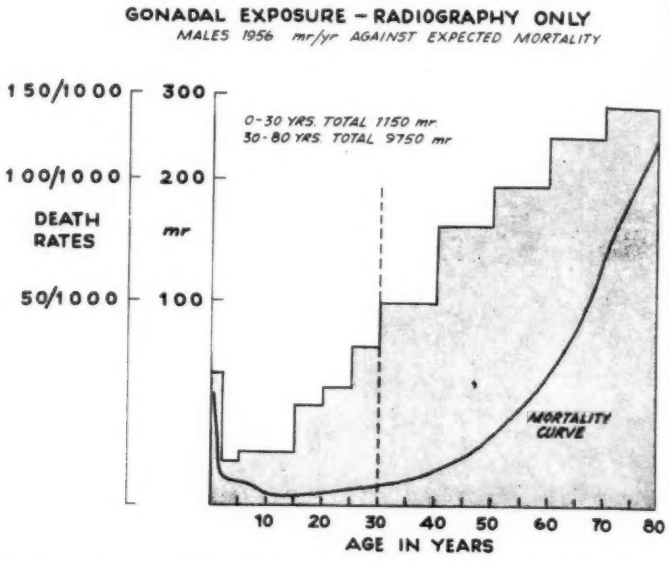
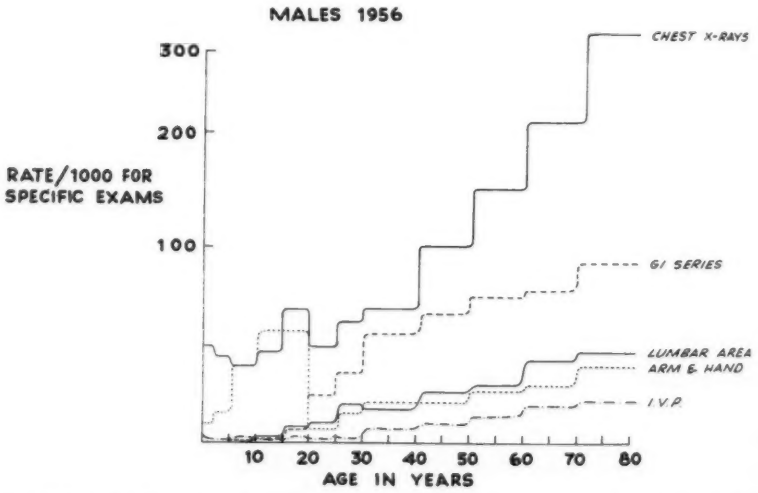


Graph 1. The milliroentgen gonadal exposure per year correlated with the standard mortality curve.



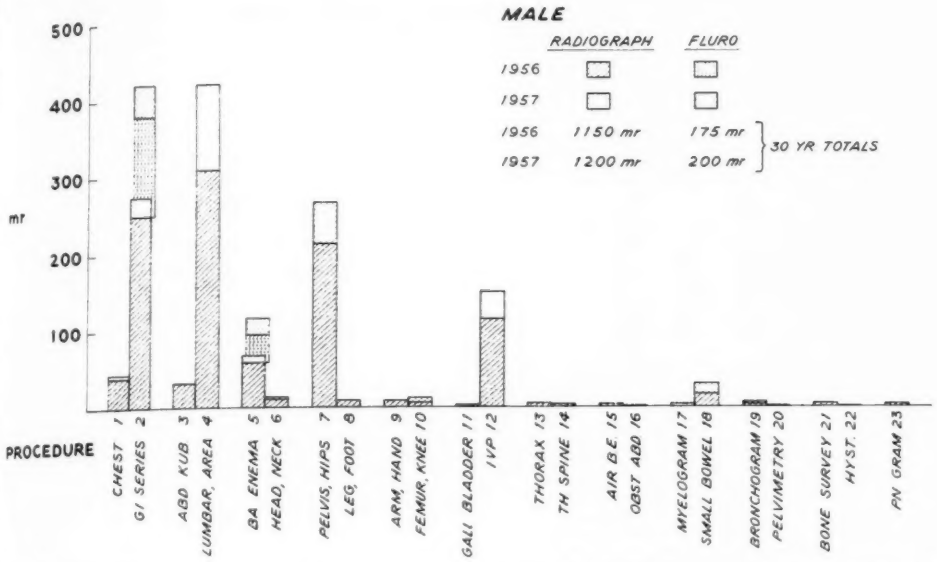
Graph 2. The frequency of selected examinations against the age of the individuals.

METHODS

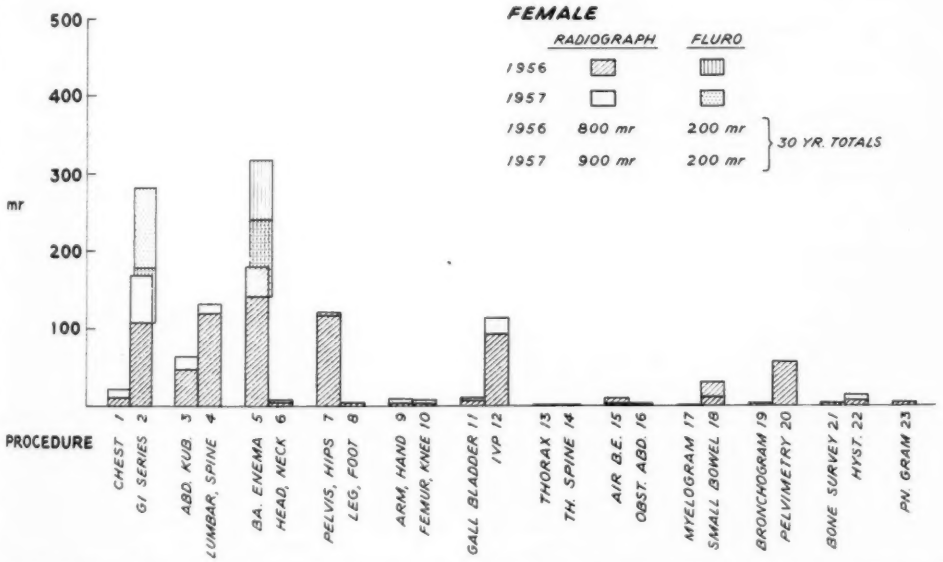
The group selected for this study were all members, for the full year studied, of the Kaiser Foundation Health Plan, which offers complete medical care to its registrants; thus any socio-economic bias is minimized. The study covered 2 consecutive years.

No restrictions on the use of diagnostic radiology were practiced in any clinic of the facility studied. Thus, as far as could be determined, the results reflect the radiological needs of the sample in a Plan where a high percentage of the attending physicians are specialists.

The age and sex distribution shown



Graph 3. Gonadal exposure from each procedure for the first thirty years, apportioned to a hypothetical individual male.



Graph 4. Gonadal exposure from each procedure for the first thirty years apportioned to a hypothetical individual female.

in Tables I and II is similar in make-up to the population of California except that in the groups aged 65 or older the number of registrants is relatively less than in the general population.

The examination designations and age groups of Tables I and II are those recommended by the International Commission on Radiological Protection Study Group. In these tables the number of procedures

TABLE I: DISTRIBUTION OF X-RAY EXAMINATIONS BY AGE, SEX, AND AREA (1956) <30 52,708 >30 57,139

Group Totals ⟶	M	2,734	4,117	6,642	5,105	2,132	1,714	3,057	9,387	8,333	6,131	3,331	837
	F	2,533	3,919	6,283	4,860	2,709	2,861	4,042	10,831	8,683	6,303	2,933	390
Age Group ⟶		0–2	2–4	5–9	10–14	15–19	20–24	25–29	30–39	40–49	50–59	60–69	70–100
01 Chest	M	113	145	195	192	131	70	164	571	846	894	701	273
	F	74	122	131	125	158	197	329	993	918	843	502	88
02 Gastrointestinal series	M	0	0	2	8	10	31	84	408	482	419	237	73
	F	2	5	8	4	10	8	40	256	284	355	205	40
03 Abdomen, kidney, ureter, bladder	M	26	18	8	4	3	6	11	61	77	95	63	16
	F	10	20	8	7	8	8	30	135	91	64	43	16
04 Lumbar area	M	4	3	4	14	14	13	43	118	166	140	113	31
	F	1	3	6	7	14	12	30	157	232	192	98	16
05 Barium enema	M	7	10	6	2	0	2	16	83	137	169	124	30
	F	10	2	4	6	16	6	27	140	216	205	137	28
06 Head and neck	M	44	49	106	93	41	15	29	142	188	188	94	38
	F	21	41	44	47	25	26	45	220	251	201	97	12
07 Pelvis, hips	M	50	20	38	26	16	5	6	35	58	48	48	15
	F	148	20	12	21	6	8	20	72	96	97	67	20
08 Leg and foot	M	18	42	100	141	69	38	49	137	144	123	56	12
	F	15	15	87	79	89	20	44	180	263	260	120	12
09 Arm and hand	M	22	54	210	250	104	13	39	144	140	125	75	27
	F	16	53	131	168	45	24	24	150	191	189	106	19
10 Femur, knee	M	2	26	52	85	46	13	22	103	75	96	46	20
	F	0	11	24	44	31	25	12	59	116	83	65	14
11 Gallbladder	M	0	0	2	0	0	1	9	42	62	68	49	7
	F	0	0	3	0	2	5	16	71	110	117	59	2
12 Intravenous pyelogram, cystogram	M	4	3	11	10	6	2	9	52	62	70	49	14
	F	0	9	20	7	4	8	21	68	79	58	26	8
13 Thorax	M	7	16	25	30	19	7	16	90	119	114	61	19
	F	9	12	11	9	5	3	16	79	102	136	72	15
14 Thoracic spine	M	3	0	3	8	2	9	13	59	69	60	47	12
	F	4	2	3	13	9	5	7	91	105	87	45	12
15 Air barium enema	M	0	0	1	0	0	0	0	8	24	32	20	5
	F	0	0	0	0	0	2	0	9	18	16	8	2
16 Obstetrical abdomen	M	..	..	..	..	..	..	..	..	..	..	..	..
	F	0	0	0	0	1	1	3	15	0	0	0	0
17 Myelogram	M	0	0	0	0	0	0	0	14	18	12	6	0
	F	0	0	0	0	0	0	0	14	28	14	0	0
18 Small bowel	M	0	0	0	0	0	6	2	12	5	14	5	0
	F	0	0	0	0	6	4	0	10	6	10	2	1
19 Bronchogram	M	0	0	0	2	0	2	0	6	12	10	12	2
	F	0	0	0	0	2	0	0	8	4	6	0	0
20 Pelvimetry	M	..	..	..	..	..	..	..	..	..	..	..	..
	F	..	..	..	1	4	6	7	11	0	0	0	0
21 Bone survey	M	7	1	4	1	0	0	1	2	1	3	2	0
	F	6	2	0	1	0	0	0	1	0	1	1	0
22 Hysterosalpingogram	M	..	..	..	..	..	..	..	..	..	..	..	..
	F	..	..	..	..	0	0	2	3	0	0	0	0
23 Pneumogram	M	1	2	0	2	0	0	1	1	3	2	2	0
	F	0	0	0	0	1	0	2	5	3	2	1	0

is tabulated from the records of the years 1956 and 1957. Tables III and IV are conversions of these first two tables, giving the results as rates per thousand registrants. Tables V and VI are constructed with use of the "probable average gonadal exposure per examination" of Laughlin and Pullman, multiplying this figure by the rate per thousand of Tables III and IV. Thus Tables V and VI state the estimated gonadal dose per thousand registrants from each type of examination, with this method of calculation.

From the preceding tables, Graph 1 was compiled to show the individual gonadal dose per year from all examinations. The relatively high dose of the first year is due not to a higher rate of examination but to the assumption by Laughlin that examinations at this age include the gonads in the primary beam. Superimposed on the chart is a line representing the standard mortality curve. This curve shows the correlation and relationship, as would be expected, between death and the use of diagnostic x-rays as an expression of illness.

Graph 2 shows the rates per thousand

TABLE II: DISTRIBUTION OF X-RAY EXAMINATIONS BY AGE, SEX, AND AREA (1957)

Group Totals ⟶	M	2,659	4,135	6,649	5,551	2,815	1,473	2,798	9,219	8,493	6,341	3,671	1,024
	F	2,528	3,922	6,257	5,301	3,146	2,623	3,768	10,792	8,919	6,535	3,313	519
Age Group ⟶		0–2	2–4	5–9	10–14	15–19	20–24	25–29	30–39	40–49	50–59	60–69	70–100
01 Chest	M	116	170	181	202	207	133	357	1,594	1,842	1,695	1,298	410
	F	104	139	146	164	270	404	593	2,148	2,322	1,869	1,121	161
02 Gastrointestinal series	M	2	6	16	28	8	24	83	462	539	484	366	84
	F	6	4	16	6	6	26	52	297	419	387	236	40
03 Abdomen, kidney, ureter, bladder	M	13	16	14	19	10	1	20	77	124	115	97	28
	F	5	20	14	9	10	16	34	134	93	92	46	15
04 Lumbar area	M	5	5	9	18	22	21	37	160	203	183	111	28
	F	2	2	4	18	27	19	28	190	258	215	143	21
05 Barium enema	M	8	6	8	10	4	2	13	87	204	183	145	76
	F	0	8	7	6	10	6	21	143	257	237	187	28
06 Head and neck	M	45	59	85	71	58	29	43	160	194	137	105	38
	F	27	31	51	44	31	24	39	174	217	201	95	13
07 Pelvis, hips	M	24	21	25	22	19	3	7	44	56	84	56	28
	F	98	53	20	14	14	7	15	41	95	82	120	19
08 Leg and foot	M	26	43	74	172	93	40	44	140	178	139	73	20
	F	7	41	86	124	60	38	35	205	239	286	144	16
09 Arm and hand	M	28	63	245	411	173	45	45	211	198	126	67	20
	F	19	78	198	134	52	19	41	171	189	231	125	20
10 Femur, knee	M	20	20	33	87	41	18	14	65	107	88	57	13
	F	7	18	5	28	21	11	6	71	88	107	90	15
11 Gallbladder	M	0	0	0	0	0	3	5	51	67	72	75	15
	F	0	2	0	0	6	11	18	85	117	136	92	12
12 Intravenous pyelogram, cystogram	M	6	5	4	19	9	2	13	66	57	67	71	22
	F	1	8	23	9	8	17	14	77	69	64	30	10
13 Thorax	M	9	13	15	36	17	7	18	81	114	131	70	24
	F	3	22	10	13	10	6	12	97	107	141	84	14
14 Thoracic spine	M	3	5	7	3	4	7	7	52	78	50	45	8
	F	0	6	3	12	6	5	5	47	70	76	64	10
15 Air barium enema	M	0	2	0	0	0	0	2	4	10	12	20	2
	F	0	0	0	0	0	0	0	8	19	4	12	0
16 Obstetrical abdomen	M	..	..	..	..	..	..	..	..	..	..	..	..
	F	..	..	..	..	..	1	6	9	1	0	0	0
17 Myelogram	M	..	..	2	0	2	0	0	14	22	18	6	0
	F	..	..	0	0	0	0	4	3	14	6	2	0
18 Small bowel	M	..	..	0	4	0	2	3	4	12	8	2	1
	F	..	..	0	0	0	0	4	6	8	11	6	0
19 Bronchogram	M	..	..	0	0	0	0	0	4	6	6	10	0
	F	..	..	0	0	0	0	2	4	2	10	2	0
20 Pelvimetry	M	..	..	..	..	..	..	..	..	..	..	..	..
	F	..	..	..	..	2	5	8	8	0	0	0	0
21 Bone survey	M	3	1	3	1	0	0	1	0	0	0	1	1
	F	0	3	0	0	0	0	0	1	1	2	2	0
22 Hysterosalpingogram	M	..	..	..	..	..	..	..	..	..	..	..	..
	F	..	..	..	..	0	0	5	10	0	0	0	0
23 Pneumogram	M	0	1	1	1	0	0	1	1	7	3	2	1
	F	1	1	0	0	1	0	1	1	0	0	1	0

examinations of selected types at different ages and illustrates the wide variations of particular examinations with age. As expected, the increased fracture period of adolescence is well documented.

Graphs 3 and 4 are compilations of the gonadal exposure from each procedure for the first thirty years, apportioned to hypothetical individual male and female, with the data from the two-year study being used as the basis for the construction.

RESULTS

Evaluation of the data yields an estimated gonadal dose of approximately 1.2 r per person for the first thirty years. If the fetal component is considered, this figure would be from 1.2 to 1.5 r. The range of the examination rates is suggested by Tables III and IV.

In Graphs 3 and 4 the contribution to the gonads from examinations in which these are directly irradiated and from those that contribute only scattered radiation is readily apparent. In fact, only two broad categories of examinations exist; those that directly irradiate the gonads and those that do not. Direct exposures

TABLE III: DISTRIBUTION OF X-RAY EXAMINATIONS BY AGE, SEX, AND AREA: EXPRESSED RATES OF EXAMINATIONS PER THOUSAND POPULATION (1956)

Age Group ⟶		0–2	2–4	5–9	10–14	15–19	20–24	25–29	30–39	40–49	50–59	60–69	70–100
01 Chest	M	41.33	35.21	29.35	37.61	61.44	40.84	53.64	60.82	101.52	145.81	210.44	326.16
	F	29.21	31.13	20.84	25.72	58.32	68.85	81.39	91.68	105.72	133.74	171.15	225.64
02 Gastrointestinal series	M	0	0	0.30	1.56	4.69	18.08	27.47	43.46	57.84	68.34	71.14	87.21
	F	0.78	1.27	1.27	0.82	3.69	2.79	9.89	23.63	32.70	56.32	69.89	102.56
03 Abdomen, kidney, ureter, bladder	M	9.50	4.37	1.20	0.78	1.40	3.50	3.59	6.49	9.24	15.49	18.91	19.11
	F	3.94	5.10	1.27	1.44	2.95	2.79	7.42	12.46	10.48	10.15	14.66	41.02
04 Lumbar area	M	1.46	0.72	0.60	2.74	6.56	7.58	14.06	12.57	19.92	22.83	33.92	37.03
	F	0.39	0.76	0.95	1.44	5.16	4.19	7.42	14.49	26.71	30.46	33.41	41.02
05 Barium enema	M	2.56	2.42	0.90	0.39	0	1.16	5.23	8.84	16.44	27.56	37.22	46.59
	F	3.94	0.51	0.63	1.23	5.90	2.09	6.67	12.92	24.87	32.52	46.70	71.78
06 Head and neck	M	16.09	11.90	15.95	18.21	19.23	8.75	9.48	15.12	22.56	30.66	28.21	45.40
	F	8.29	10.46	7.00	9.67	9.22	9.08	11.13	20.31	28.90	31.88	33.07	30.76
07 Pelvis, hips	M	18.28	4.85	5.72	5.09	7.50	2.91	1.96	3.72	6.96	7.82	14.41	17.92
	F	58.42	5.10	1.90	4.32	2.21	2.79	4.94	6.64	11.05	15.38	22.84	51.28
08 Leg and foot	M	6.58	10.20	15.05	27.61	32.36	22.17	16.02	14.59	17.28	20.06	16.81	14.33
	F	5.92	3.82	13.84	16.25	32.85	6.99	10.88	16.61	30.28	41.25	40.91	30.76
09 Arm and hand	M	8.04	13.11	31.61	48.97	48.78	7.58	12.75	15.34	16.80	20.38	22.51	32.25
	F	6.31	13.52	20.84	34.56	16.61	8.38	5.93	13.84	21.99	29.98	36.14	48.71
10 Femur, knee	M	0.73	6.31	7.82	16.65	21.57	7.58	7.19	10.97	9.00	15.65	13.80	23.89
	F	0	2.80	3.81	9.05	11.44	8.73	2.96	5.44	13.35	13.16	22.16	35.89
11 Gallbladder	M	0	0	0.30	0	0	0.58	2.94	4.47	7.44	11.09	14.71	8.36
	F	0	0	0.47	0	0.73	1.74	3.95	6.55	12.66	18.56	20.11	5.12
12 Intravenous pyelogram, cystogram	M	1.46	0.72	1.65	1.95	2.81	1.16	2.94	5.53	7.44	11.41	14.71	16.72
	F	0	2.29	3.18	1.44	1.47	2.79	5.19	6.27	9.09	9.20	8.86	20.51
13 Thorax	M	2.56	3.88	3.76	5.87	8.91	4.08	5.23	9.58	14.28	18.59	18.31	23.70
	F	3.55	3.06	1.75	1.85	1.84	1.04	3.95	7.29	11.74	21.57	24.54	38.46
14 Thoracic spine	M	1.09	0	0.45	1.56	0.93	5.25	4.25	6.28	8.28	9.78	14.10	14.33
	F	1.57	0.51	0.47	2.67	3.32	1.74	1.73	8.40	12.09	13.80	15.34	30.76
15 Air barium enema	M	0	0	0.15	0	0	0	0	0.85	2.88	5.21	6.00	5.97
	F	0	0	0	0	0	0.69	0	0.83	2.07	2.53	2.72	5.12
16 Obstetrical abdomen	M	...	...	...	...	...	...	...	...	...	...	...	...
	F	0	0	0	0	0.36	0.34	0.74	1.38	0	0	0	0
17 Myelogram	M	0	0	0	0	0	0	0	1.49	2.16	1.95	1.80	0
	F	0	0	0	0	0	0	0	1.29	3.22	2.22	0	0
18 Small bowel	M	0	0	0	0	0	3.50	0.65	1.27	0.60	2.28	1.50	0
	F	0	0	0	0	2.21	1.39	0	0.92	0.69	1.58	0.68	10.25
19 Bronchogram	M	0	0	0	0.39	0	1.16	0	0.63	1.44	1.63	3.60	2.38
	F	0	0	0	0	0.73	0	0	0.73	0.46	0.95	0	0
20 Pelvimetry	M	...	...	...	...	...	...	...	...	...	...	...	...
	F	...	...	...	0.20	1.47	2.09	1.73	1.01	0	0	0	0
21 Bone survey	M	2.56	0.24	0.60	0.19	0	0	0.32	0.21	0.12	0.48	0.60	0
	F	2.36	0.51	0	0.20	0	0	0	0.09	0	0.15	0.34	0
22 Hysterosalpingogram	M	...	...	...	...	...	...	...	...	...	...	...	...
	F	...	...	...	...	0	0	0.49	0.27	0	0	0	0
23 Pneumogram	M	0.36	0.48	0	0.39	0	0	0.32	0.10	0.36	0.32	0.60	0
	F	0	0	0	0	0.36	0	0.49	0.46	0.34	0.31	0.34	0

may give a hundred times as much radiation to the gonads per examination. Thus, it is possible to make generous assumptions in the nondirect examinations and yet produce little error in the total gonadal dose. An important example is furnished by chest roentgenograms, estimated in the Laughlin report to number 3.2 million per year, with a gonadal exposure of only 2,500 r out of a total of 11 million r per year. The significant examinations, then, are relatively few in number and some degree of accuracy is desirable if the total estimate is to be reliable. These facts also emphasize the need for proper technics in order that those examinations presumed not to include the gonads may be so conducted as to adhere to this presumption.

The possibility of greatly reducing the gonadal exposure by altering the criteria for requesting roentgen studies would appear questionable if the present graphs are reliable. Examinations of the chest, for instance, which constitute a large percentage of the whole, involve so little gonadal exposure that, even if they were prohibited, the total would be little

TABLE IV: DISTRIBUTION OF X-RAY EXAMINATIONS BY AGE, SEX, AND AREA: EXPRESSED RATES OF EXAMINATIONS PER THOUSAND POPULATION (1957)

Age Group →		0–2	2–4	5–9	10–14	15–19	20–24	25–29	30–39	40–49	50–59	60–69	70–100
01 Chest	M	43.62	41.11	27.22	36.38	73.53	90.29	127.59	172.90	216.88	267.30	353.58	400.39
	F	41.13	35.44	23.33	30.93	85.82	154.02	157.37	199.03	260.34	285.99	338.36	310.21
02 Gastrointestinal series	M	0.75	1.45	2.40	5.04	2.84	16.29	29.66	50.11	60.43	76.32	99.70	82.03
	F	2.37	1.01	2.55	1.13	1.90	9.91	13.80	27.52	46.97	59.21	71.23	77.07
03 Abdomen, kidney, ureter, bladder	M	4.88	3.86	2.10	3.42	3.55	0.67	7.14	8.35	14.60	18.13	26.42	27.34
	F	1.97	5.09	2.23	1.69	3.17	6.09	9.02	12.41	10.42	14.07	13.88	28.90
04 Lumbar area	M	1.88	1.20	1.35	3.24	7.81	14.25	13.22	17.35	23.90	28.85	30.23	27.34
	F	0.79	0.50	0.63	3.39	8.58	7.24	7.43	17.60	28.92	32.89	43.16	40.46
05 Barium enema	M	3.00	1.45	1.20	1.80	1.42	1.35	4.64	9.43	24.01	28.85	39.49	74.21
	F	0	2.03	1.11	1.13	3.17	2.28	5.57	13.25	28.81	36.26	56.44	53.94
06 Head and neck	M	16.92	14.26	12.78	12.79	20.60	19.68	15.36	17.35	22.84	21.60	28.60	37.10
	F	10.68	7.90	8.15	8.30	9.85	9.14	10.35	16.12	24.33	30.75	28.68	25.04
07 Pelvis, hips	M	9.02	5.07	3.75	3.96	6.74	2.03	2.50	4.77	6.59	13.24	15.26	27.34
	F	38.76	13.51	3.19	2.64	4.45	2.66	3.98	3.79	10.65	12.54	36.22	36.60
08 Leg and foot	M	9.77	10.39	11.12	30.98	33.03	27.15	15.72	15.18	20.95	21.92	19.88	19.53
	F	2.76	10.45	13.74	23.39	19.07	14.48	9.28	18.99	26.79	43.76	43.46	30.82
09 Arm and hand	M	10.53	15.23	36.84	74.04	61.45	30.54	16.08	22.88	23.31	19.87	18.25	19.53
	F	7.51	19.88	31.64	25.27	16.52	7.24	10.88	15.84	21.19	35.34	37.73	38.53
10 Femur, knee	M	7.52	4.83	4.96	15.67	14.56	12.21	5.00	7.05	12.59	13.87	15.52	12.69
	F	2.76	4.58	0.79	5.28	6.67	4.19	1.59	6.57	9.86	16.37	27.16	28.90
11 Gallbladder	M	0	0	0	0	0	2.03	1.78	5.53	7.88	11.35	20.43	14.64
	F	0	0.50	0	0	1.90	4.19	4.77	7.87	13.11	20.81	27.76	23.12
12 Intravenous pyelogram, cystogram	M	2.25	1.20	0.60	3.42	3.19	1.35	4.64	7.15	6.71	10.56	19.34	21.48
	F	0.39	2.03	3.68	1.69	2.54	6.48	3.71	7.13	7.73	9.79	9.05	19.26
13 Thorax	M	3.38	3.14	2.25	6.48	6.03	4.75	6.43	8.78	13.42	20.65	19.06	23.43
	F	1.18	5.60	1.59	2.45	3.17	2.28	3.18	8.98	11.99	21.57	25.35	26.97
14 Thoracic spine	M	1.12	1.20	1.05	0.54	1.42	4.75	2.50	5.64	9.18	7.88	12.25	7.81
	F	0	1.52	0.47	2.26	1.90	1.90	1.32	4.35	7.84	11.62	19.31	19.26
15 Air barium enema	M	0	0.48	0	0	0	0	0.71	0.43	1.17	1.89	5.44	1.95
	F	0	0	0	0	0	0	0	0.74	2.13	0.61	3.62	0
16 Obstetrical abdomen	M	...	...	...	...	...	...	...	...	...	...	...	...
	F	...	...	...	...	...	0.38	1.59	0.83	0.11	0	0	0
17 Myelogram	M	...	...	0.30	0	0.71	0	0	1.51	2.59	2.83	1.63	0
	F	...	...	0	0	0	0	1.06	0.27	1.56	0.91	0.60	0
18 Small bowel	M	...	...	0	0.72	0	1.35	1.07	0.43	1.41	1.26	0.54	0.97
	F	...	...	0	0	0	0	1.06	0.55	0.89	1.68	1.81	0
19 Bronchogram	M	...	...	0	0	0	0	0	0.43	0.70	0.94	2.72	0
	F	...	...	0	0	0	0	0.53	0.37	0.22	1.53	0.60	0
20 Pelvimetry	M	...	...	...	...	...	...	...	...	...	...	...	...
	F	...	...	...	...	0.63	1.90	2.12	0.74	0	0	0	0
21 Bone survey	M	1.12	0.24	0.45	0.18	0	0	0.35	0	0	0	0.27	0.97
	F	0	0.76	0	0	0	0	0	0.09	0.11	0.30	0.60	0
22 Hysterosalpingogram	M	...	...	...	...	...	...	...	...	...	...	...	...
	F	...	...	...	...	0	0	1.32	0.92	0	0	0	0
23 Pneumogram	M	0	0.24	0.15	0.18	0	0	0.35	0.10	0.82	0.47	0.54	0.97
	F	0.39	0.25	0	0	0.31	0	0.26	0.09	0	0	0.30	0

affected. The radiologic examinations that result in the greatest exposure are nearly always done for specific symptoms and are usually essential to determine their etiology. (This does not mean that we condone indiscriminate use of x-rays for diagnosis.)

Although standards for radiographic equipment will be established by State regulations, it is difficult to assess their importance in reducing the gonadal exposure. The use of antiquated machines, without filtration and cones, certainly results in greatly increased gonadal dose. The number of such installations is not known, but more information will certainly become available as States register and survey radiation sources.

Physicians should make sure that their installations meet the recommendations of National Bureau of Standards *Handbook 60* so that, as developments proceed, no grounds for criticism or justification for punitive control can be established.

Perhaps the most important factor in achieving a significant reduction in gonadal exposure, or in maintaining the exposure at a minimum without sacrificing adequate

TABLE V: MR/1,000 FROM X-RAY EXAMINATIONS BY AGE, SEX, AND AREA (1956)

Age Group →			0-2	2-4	5-9	10-14	15-19	20-24	25-29	30-39	40-49	50-59	60-69	70-100	
01	Chest	M	18,598	176	146	45	73	49	64	73	122	174	252	391	
		F	7,039	155	104	7	17	20	24	27	32	40	51	67	
02	Gastrointestinal series	M	0	0	300	1,482	4,445	17,176	26,096	41,287	54,948	64,923	67,583	82,849	
		F	1,170	1,905	1,905	861	3,874	2,929	10,384	24,811	34,335	59,136	73,384	107,688	
03	Abdomen, kidney, ureter, bladder	M	4,275	8,005	900	156	280	700	718	1,298	1,848	3,098	3,782	3,822	
		F	945	1,989	914	720	1,475	1,395	3,710	6,230	5,240	5,075	7,330	20,310	
04	Lumbar area	M	3,942	1,728	1,440	5,480	13,120	15,160	28,120	25,140	39,840	45,660	67,840	74,060	
		F	351	798	1,187	1,440	5,160	4,190	7,410	14,490	26,710	30,460	33,410	41,020	
05	Barium enema	M	3,072	4,840	1,350	3,705	0	1,102	4,968	8,398	15,618	26,182	35,359	44,260	
		F	6,855	867	1,386	2,460	11,800	4,180	13,340	25,840	49,740	65,040	93,100	143,580	
06	Head and neck	M	7,240	59	9	10	11	5	5	9	13	18	16	27	
		F	1,989	52	1	1	1	1	2	4	5	6	6	6	
07	Pelvis, hips	M	8,774	4,074	11,440	10,180	15,000	5,820	3,920	7,440	13,920	15,640	28,820	35,840	
		F	15,773	2,142	1,710	4,320	2,210	2,790	4,940	6,640	11,050	15,380	22,810	51,280	
08	Leg and foot	M	2,961	51	75	27	32	22	16	14	17	20	16	14	
		F	1,420	19	69	8	16	3	5	8	15	20	20	15	
09	Arm and hand	M	3,618	65	48	48	49	7	12	15	16	20	22	32	
		F	1,514	67	104	17	8	4	3	6	10	14	18	24	
10	Femur, knee	M	328	31	39	16	21	7	7	10	9	15	13	23	
		F	0	14	19	4	5	4	1	2	6	6	11	17	
11	Gallbladder	M	0	0	3	0	0	5	29	44	74	110	147	83	
		F	0	0	94	0	146	348	790	1,310	2,332	3,712	4,022	1,024	
12	Intravenous pyelogram, cystogram	M	2,920	1,440	3,300	3,900	5,620	2,320	5,880	11,060	14,880	22,820	29,420	33,440	
		F	0	2,748	3,816	1,728	1,764	3,348	6,228	7,524	10,908	11,040	10,632	24,612	
13	Thorax	M	1,152	19	18	5	8	4	5	9	14	18	18	22	
		F	887	15	8	...	...	1	2	3	5	10	12	19	
14	Thoracic spine	M	491	0	2	1	1	5	4	6	8	9	14	14	
		F	376	2	2	1	2	1	1	4	6	6	7	15	
15	Air barium enema	M	0	0	225	0	0	0	0	1,275	4,320	7,815	9,000	8,955	
		F	0	0	0	0	0	1,380	0	1,660	4,140	5,060	5,440	10,240	
16	Obstetrical abdomen	M	..	....	....	....	....	....	....	....	....	....	....	....	
		F	0	0	0	0	93	88	192	358	0	0	0	0	
17	Myelogram	M	0	0	0	0	0	0	0	....	....	....	....	0	
		F	0	0	0	0	0	0	0	....	....	....	0	0	
18	Small bowel	M	0	0	0	0	0	5,250	975	1,905	900	3,420	2,250	0	
		F	0	0	0	0	4,420	2,780	0	1,840	1,380	3,160	1,360	20,500	
19	Bronchogram	M	0	0	0	195	0	580	0	315	720	815	1,800	1,190	
		F	0	0	0	0	547	0	0	547	345	712	0	0	
20	Pelvimetry	M	....	....	....	....	....	....	....	....	....	....	....	....	
		F	....	....	....	500	3,675	5,225	4,325	2,525	0	0	0	0	
21	Bone survey	M	1,152	1	3	....	0	0	1	....	....	....	....	0	
		F	566	2	0	1	0	0	0	....	0	0	....	0	
22	Hysterosalpingogram	M	..	....	....	....	....	....	....	....	....	....	....	....	
		F	....	....	....	....	0	0	1,225	675	0	0	0	0	
23	Pneumogram	M	720	9	0	1	0	0	1	....	1	....	1	0	
		F	0	0	0	0	1	0	1	....	....	....	....	0	

diagnostic examination, is the skill with which the proper equipment, cones, and filters are used, insuring that only the field of interest is exposed to the primary radiation and that the films correctly delineate the area desired. Where the male gonads are directly in the primary beam, gonadal shielding should become a standard, required, routine part of the preparation of the patient. Further development of a convenient, efficient shield is well justified, and its use would be merited in such examinations.

The constant striving of the medical profession for improvement in technic and reduction of dose is extensively documented and is the most important force for increasing the proficiency of the examiner and in achieving new developments and improvements of training and equipment. Such efforts should receive encouragement and support in any State program constructed to maintain minimal gonadal exposure in diagnostic radiology.

In the opening paragraphs, above, the probable estimate of 4.0 r was presented

TABLE VI: MR/1,000 FROM X-RAY EXAMINATIONS BY AGE, SEX, AND AREA (1957)

Age Groups ⟶		0–2	2–4	5–9	10–14	15–19	20–24	25–29	30–39	40–49	50–59	60–69	70–100
01 Chest	M	19,629	205	136	43	88	108	153	207	260	347	424	480
	F	9,871	177	116	9	25	46	47	59	78	85	101	93
02 Gastrointestinal series	M	750	1,450	2,400	4,788	2,698	15,475	28,177	47,604	57,408	72,504	94,715	77,928
	F	3,555	1,515	3,825	1,186	1,995	10,405	14,490	28,896	49,318	62,170	74,791	80,923
03 Abdomen, kidney, ureter, bladder	M	2,196	3,589	1,575	684	710	134	1,428	1,670	2,920	3,626	5,284	5,468
	F	472	1,985	1,605	845	1,585	3,045	4,510	6,205	5,210	7,035	6,940	14,450
04 Lumbar area	M	5,076	2,880	3,240	6,480	15,620	28,500	26,440	34,700	47,800	57,700	60,460	54,680
	F	711	525	787	3,390	8,580	7,240	7,430	17,600	28,920	32,890	43,160	40,460
05 Barium enema	M	3,600	2,900	1,800	1,710	1,349	1,282	4,408	8,958	22,809	27,407	37,515	70,499
	F	0	3,451	2,442	2,260	6,340	4,560	11,140	26,500	57,620	72,520	112,880	107,880
06 Head and neck	M	7,614	71	7	7	12	11	9	10	13	12	17	22
	F	2,563	39	1	1	1	1	2	3	4	6	5	5
07 Pelvis, hips	M	4,329	4,258	7,875	7,920	13,480	4,060	5,000	9,540	13,180	26,480	30,520	54,680
	F	10,465	5,674	2,871	2,640	4,450	2,660	3,980	3,790	10,650	12,540	36,220	36,600
08 Leg and foot	M	4,396	51	55	30	33	27	15	15	20	21	19	19
	F	662	52	68	11	9	7	4	9	13	21	21	15
09 Arm and hand	M	4,738	76	184	74	61	30	16	22	23	19	18	19
	F	1,802	99	158	12	8	3	5	7	10	17	18	19
10 Femur, knee	M	3,384	24	24	15	14	12	5	7	12	13	15	12
	F	662	22	3	2	3	2	...	3	4	8	13	14
11 Gallbladder	M	0	0	0	0	0	20	17	55	78	113	204	146
	F	0	...	0	0	380	838	954	1,574	2,622	4,162	5,552	4,624
12 Intravenous pyelogram, cystogram	M	4,500	2,400	1,200	6,840	6,380	2,700	9,280	14,300	13,420	21,120	38,680	42,960
	F	468	2,842	4,416	2,028	3,048	7,776	4,452	8,556	9,276	11,748	10,860	23,112
13 Thorax	M	1,521	15	11	6	6	4	6	8	13	20	19	23
	F	295	28	7	1	1	1	1	4	5	10	12	13
14 Thoracic spine	M	504	6	5	...	1	4	2	5	9	7	12	7
	F	0	7	2	1	...	...	...	2	3	5	9	9
15 Air barium enema	M	0	2	0	0	0	0	...	645	1,755	2,835	8,160	2,925
	F	0	0	0	0	0	0	0	1,480	4,260	1,220	7,240	0
16 Obstetrical abdomen	M	...	...	...	...	...	...	...	...	...	...	...	...
	F	...	...	...	...	...	98	413	215	28	0	0	0
17 Myelogram	M	...	...	...	0	...	0	0	...	...	...	...	0
	F	...	...	0	0	0	0	...	...	...	...	...	0
18 Small bowel	M	...	...	0	...	0	2,025	1,605	645	2,115	1,890	810	1,455
	F	...	...	0	0	0	0	2,120	1,100	1,800	3,360	3,620	0
19 Bronchogram	M	...	...	0	0	0	0	0	215	350	470	1,360	0
	F	...	...	0	0	0	0	397	277	165	1,147	450	0
20 Pelvimetry	M	...	...	...	...	...	...	...	...	...	...	...	...
	F	...	...	...	...	1,575	4,750	5,300	1,850	0	0	0	0
21 Bone survey	M	504	1	2	...	0	0	...	0	0	0	...	...
	F	0	3	0	0	0	0	0	...	...	...	...	0
22 Hysterosalpingogram	M	...	...	...	...	...	...	...	...	...	...	...	...
	F	..	...	...	...	0	0	3,300	2,300	0	0	0	0
23 Pneumogram	M	0	4	3	...	0	0	1	...	2	1	1	2
	F	780	5	0	0	...	0	...	...	0	0	...	0

as an unreliable figure. On the basis of this investigation, the probable estimate would be at the lower limits of the National Academy of Sciences figures, namely about 1.5 r. If the "average exposure estimates" of Webster and Merrill were employed, the estimate would be further reduced by as much as 50 per cent. The validity of changes in the compilation of the estimate may be questionable, but the present distribution pattern appears to have at least equal, if not greater, validity as the assumptions used in making the National Academy of Sciences estimate. The latter distribution pattern was, in general, derived by estimating the total examinations and then applying the percentage distribution of radiologic examinations from previously published literature. In some examinations, such as pelvimetry, special investigations were made, but a certain bias was admitted, as evidenced by the following quotation from the Laughlin-Pullman report:

"It is true that the hospitals in this survey are particularly interested in pelvimetry. The frequency

of pelvimetry averaged over primiparae and multiparae range from 3 to 25 per cent and the overall average of 11 per cent will be used for the national average."

By way of comparison, our two-year study included 5,030 births and 52 pelvimetries. If the above quoted estimates were used, an estimate of 550 pelvimetries would have resulted. These data, which have contributed so importantly to reports regarding gonadal exposure, will be reviewed in a separate publication.

Although the work of the National Academy of Sciences was thoughtfully performed and analyzed in great detail, the basic data representing the correct distribution for the population are questionable. For instance, the radiology in a teaching hospital represents to a degree the staff specialists using its services, *i.e.*, there may be more neurosurgeons in one large medical center than there are in some entire states. This bias must be corrected in using data on large population groups, since it is the radiology distribution per thousand of population that is desired. In addition, the number of examinations done for research or special interest must be added to the basic figure, and the magnitude of this contribution to the total dose is worthy of further determination. It would appear possible, however, that the present gonadal exposure may be in the range of the minimal figure of the Laughlin and Pullman report, and it may be well below the probable average gonadal figure of 4.0 r. Even if this possibility is rejected, a gonadal dose of below 1.5 r during the course of thirty years is readily attainable without altering the present use of diagnostic roentgenology. In fact, if radiological examinations are based on medical indications and the proper equipment and technic are used, an average gonadal dose of less than 500 mr in thirty years could be achieved.

SUMMARY

The radiologic examinations made on 100,000 registrants of a total medical care health plan were analyzed for two consecutive years. On the basis of Laughlin and Pullman's estimated dose per examination, the total gonadal exposure per person, up to the age of thirty years, was calculated as 1.2 to 1.5 r.

It is suggested that the basic data used in the present study are as reliable as those employed by the various authors for estimates published in 1956 by the National Academy of Sciences. This assumption would lead to the conclusion that the gonadal exposure up to age thirty of the population of the United States lies below the 4.5 r "probable average" widely used and quoted by those interested in radiation protection.

If it is possible to maintain total rates of examinations (assuming distribution as found in this study) and maintain good technic, then 500 mr is suggested as a realistic average gonadal exposure limit from diagnostic radiology up to the age of thirty. Such exposure is possible without changing the present medical indications for such studies.

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SUMMARIO IN INTERLINGUA

Le Numero e le Distribution del Examines Roentgenologic in un Population de 100.000 Individuos

Esseva analysate le examines radiologic effectuate in 1956 e 1957 in 100.000 participantes in un programma sanitari de assistentia medical total. Super le base del estimate dose applicate in le examine individual, il esseva calculate que le total exposition gonadal per individuo usque al etate de trenta annos amontava a inter 1,2 e 1,5 r. Si nos suppone que le datos de base in le presente studio non es minus digne de confidentia que illos usate pro estimationes publicate in 1956 per le statounitese Academia National de Scientias, nos pote concluder que le exposition gonadal usque al etate de trenta annos in le population del Statos Unite es infra le 4,5 r que es extensemente citate como "un media probabile."

Si il es possibile mantener le frequentias del examines radiologic con le distribution constatate in le presente studio e si le standards technic pote esser mantenite a un bon nivello, il pare justificate proponer 500 mr como un limite realista pro le exposition gonadal medie ab radiologia diagnostic usque al etate de trenta annos.

Nasopharyngeal Malignant Tumors: 82 Consecutive Patients Treated in a Period of Twenty-Two Years[1]

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THIS PUBLICATION is based on the study of 82 consecutive cases of malignant nasopharyngeal tumors treated from 1932 to 1954 in the Department of Radiology of the University of California, San Francisco. All were histologically verified and followed.

INCIDENCE

The incidence of malignant nasopharyngeal tumors is estimated at 1 to 2 per cent of all cancers (13, 16, 22). Of a total of 3,353 patients treated for malignant diseases at the University of California during the years covered by the study, 614 had malignant tumors of the head and neck. The 82 cases reported thus represent 2.4 per cent of 3,353 treated cancer cases and 13.3 per cent of 614 head and neck tumors (Table I).

Fifty-eight patients in the series were men (71 per cent), 24 were women: a ratio of 5:2. This coincides closely with the ratio of males and females reported by others (13, 15, 16, 25, 27) (Table II).

Digby (8), in 1941, reported a high incidence of malignant nasopharyngeal tumors among Chinese, even when compared to carcinoma of the cervix or breast. In Formosa, Yeh and Cowdry (34) discovered nasopharyngeal carcinomas to be exceeded in number only by genital cancers. This high incidence also occurs among the Indonesians of Surabaja and vicinity (9). Lenz's series from Presbyterian and Montefiore Hospitals, New York City, included 4 Chinese among 63 nasopharyngeal patients (6.4 per cent) (15). According to the 1950 census report (33), the New York City Chinese population (18,327) comprises 0.25 per cent of the total 7,891,957. Martínez (18) found that of 69 patients with nasopharyngeal cancer at the Cancer Institute of Havana, 29 per cent were Chinese. The 1943 Cuban census reported 6,539 Chinese in Havana's 659,883 population (0.99 per cent) (32). Of our 82 patients, 13 were Chinese and 1 was Korean. Nine of these patients were born in China, 1 was born in the United States, and the birthplace of 3 was not recorded. This high incidence (17 per cent) is compatible with the previously reported frequency of nasopharyngeal tumors in Chinese and the large Chinese population in San Francisco. The San Francisco Chamber of Commerce in 1957 estimated that 30,000 (3.7 per cent) of the 814,000 San Francisco inhabitants were Chinese (Table III).

The ages of our patients ranged from two to seventy-seven years, with an average of 49.6 years. The average age of the men was 49.9 years, of women 49.1 years. This figure is in agreement with those of other authors (11, 13, 15, 16, 22, 25, 27). Fifty-four of the treated patients were in the forty- to sixty-year age group (Fig. 1).

TABLE I: COMPARATIVE INCIDENCE, UNIVERSITY OF CALIFORNIA HOSPITAL, 1932–1954

Type	Number of Cases	Per Cent of Total
Head and neck (includes nasopharynx), 82 (2.4%)	614	18.4
Gynecologic	746	22.2
Other malignant tumors	1,993	59.4
TOTAL (all cases treated)	3,353	100.0

TABLE II: SEX INCIDENCE IN REPORTED SERIES

	Male	Female
University of California Hospital, San Francisco, Calif.	58 (71%)	24 (29%)
Lenz: Presbyterian & Montefiore Hospitals, New York, N. Y.	45 (71%)	18 (29%)
Martin-Blady: Memorial Hospital, New York, N. Y.	68 (78%)	19 (22%)
Scanlon: Mayo Clinic, Rochester, Minn.	70 (79%)	18 (21%)

[1] From the Department of Radiology, University of California, School of Medicine, San Francisco, Calif. Presented at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15-20, 1959.

TABLE III: RACE INCIDENCE (CAUCASIAN VS. CHINESE) IN REPORTED SERIES

	Caucasian	Chinese	Negro, Mulatto	Percentage of Chinese in the Population
University of California Hospital, San Francisco, Calif.	68 (83%)	14 (17%)	...	3.7
Lenz: Presbyterian, Montefiore Hospitals, New York, N. Y.	59 (94%)	4 (6%)	...	0.25
Martinez: Cancer Inst., Havana, Cuba	34 (49%)	20 (29%)	15 (22%)	0.99

SYMPTOMS AND SIGNS

Enlarged cervical lymph nodes constituted the initial and only complaint in 24 (29.3 per cent) of our patients and in an additional 15 were associated with other symptoms. On examination, however, cervical adenopathy was found unilaterally in 34 patients and bilaterally in 25. It was absent in only 23 patients. This high incidence of initial lymph node involvement has been uniformly reported in the literature (3, 8, 11, 13, 15, 22). Initial symptoms and signs related to the ears (deafness, fullness, earache) or to the nose (nasal obstruction, bloody discharge) occurred next in frequency (Table IV).

TABLE IV: FIRST PATIENT-RECOGNIZED SYMPTOM OR SIGN

	Number of Cases
Cervical lymphadenopathy	39 (47.5%)
Nasal obstruction, epistaxis, bloody discharge	30 (36.6%)
Earache, hypacusia	23 (28.0%)
Headache	6 (7.3%)
Cranial nerve paralysis (usually diplopia)	5 (6.1%)
Sore throat	4 (4.9%)
Facial pain	2 (2.4%)

Del Regato (7) stated that in nasopharyngeal carcinoma the cranial nerves are most often involved by (*a*) direct extension of the neoplasm, the petrosphenoidal syndrome of Jarod, and (*b*) metastatic involvement of lymph nodes

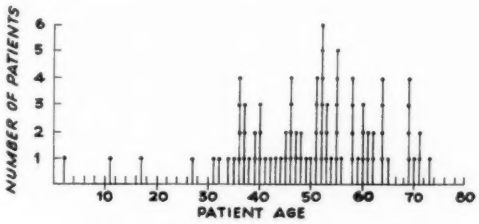

Fig. 1. Age incidence of 82 cases.

TABLE V: SIGNS PRESENT ON ADMISSION

	Number of Patients	Per Cent of Total
Cervical lymphadenopathy		
None	23	28.1
Unilateral	34	41.4
Bilateral	25	30.5
Paralysis, cranial nerves		
Petrosphenoid, alone	5	6.1
Retroparotid, alone	5	6.1
Petrosphenoid and retroparotid	9	11.0
Erosion of base of skull	9	11.0

in the retroparotid space of Villaret. Often, as in this series, both syndromes occur, usually involving nerves unilaterally. Among 19 patients with initial involvement of cranial nerves, there was evidence of both direct extension of the tumor along the petrosphenoidal route and metastases to the retroparotid group of nodes in 9. In 4 of 5 patients with involvement of the petrosphenoidal carrefour nerves alone, diplopia and internal strabismus indicated paralysis of the fourth cranial nerve only. In 5 patients, metastases occurred in the retroparotid nodes without evidence of direct extension of the neoplasm; in 2 of these, Horner's syndrome was present. The cranial nerves most commonly involved were the fifth and sixth. Lederman (14) claims that the sole sign of absence of the corneal reflex (involvement of the trigeminal nerve) is indicative of direct extension of the disease along petrosphenoidal pathways (Table V). Erosion or invasion of the base of the skull was noted on admission in 9 of the 82 patients (11 per cent), which is lower than in Martin's and Lenz's series. In the present study, however, roentgen examination of the skull was not done before treatment in 17 cases.

TABLE VI: DURATION OF SYMPTOMS BEFORE DIAGNOSIS

	Number of Cases
Three months and under	27
Three to six months	14
Six months to one year	17
One year and over	24
AVERAGE, 8 months	

Routine skull roentgenograms in 9 patients with cranial nerve involvement showed erosion or invasion of the base of the skull in 8 .

The average duration of symptoms and signs was slightly more than eight months, with half the patients having been aware of something amiss for at least six months before the diagnosis was established; in 4, symptoms were present three years (Table VI). Both women and men were equally tardy in securing adequate attention, women averaging eight and one-half months compared to the men's delay of eight months.

Frequent incorrect diagnosis or mismanagement by physicians led Cantril (5) to refer to the nasopharynx as a "diagnostic blind spot." Buschke (4) described a patient who was treated by weekly insufflations of the eustachian tube for one year; the attending physicians were not aroused until cervical adenopathy appeared. Twenty-nine of our 82 cases were misdiagnosed by physicians, and "ear lancing," "radical neck surgery," or "antrum exploration" were carried out in 14. The situation has changed little since New's report on the errors of diagnosis in this disease (21). In one patient, not included in this series, the diagnosis was established only after craniotomy (performed prior to admission here in 1954) revealed an anaplastic tumor in the left posterior and middle fossae. Postoperatively, the location of this tumor in the nasopharynx was recognized.

PATHOLOGY

Grossly, tumors of the nasopharynx may develop into three types:

1. *Ulcerated:* Most frequently located on the posterior wall or deep in Rosenmüller's fossa; characteristically compressing or invading the second, third, fourth, fifth, or sixth cranial nerves.

2. *Lobulated:* Arising most commonly from the eustachian tube area as lympho-epithelioma or undifferentiated epidermoid carcinoma. This form seldom ulcerates or grows rapidly enough to cause compression of the petrosphenoid region cranial nerves.

3. *Exophytic Nonulcerated:* Arising from the roof but, if from the pharyngeal tonsil, often filling the cavity. These tumors frequently involve the maxillary sinus and orbit. Those of eustachian tube origin spread submucosally toward the skull base and seldom produce cranial nerve paralysis. Another insidious form of exophytic lymphosarcoma may arise in the fossa of Rosenmüller and remain long hidden without obvious signs or symptoms (1).

Ackerman (1) explained well the difficulty of placing these tumors in completely acceptable histologic slots. Many pathologists question the existence of transitional-cell carcinoma or Quick's (23) "transitional-cell epidermoid carcinoma." Regaud (24) and Schmincke (26) simultaneously and separately described a new pathologic entity in 1921, the lympho-epithelioma. Stewart (29) maintains that many so-called lympho-epitheliomas are in truth lymphosarcoma. Teoh (31), after detailed necropsies in 31 cases of nasopharyngeal epidermoid carcinoma at the University of Hong Kong, concluded that so-called lympho-epitheliomas are actually epidermoid tumors and that single small biopsy specimens erroneously lead to a diagnosis of lympho-epithelioma in epidermoid carcinoma of the nasopharynx.

The histologic diagnosis often depends not only on the particular pathologist but on his past training and present reading habits, even on his mood at the time consulted. Table VII is presented in the light of these facts. The low incidence of lymphosarcoma in this series (4.9 per cent) compares well with the incidence in Geist and Portmann's (11) series (8.3 per cent)

and in the series of Kramer (13) (7.4 per cent), but is in sharp contrast to the incidence reported by Lenz (15), Baclesse (2), Nielsen (22), Martin and Blady (16), and Eberhard and Leaming (10), which ranges from 20 to 40 per cent of the totals. Our low incidence of adenocarcinoma (2.4 per cent) agrees with the majority of other reported series (11, 13, 15, 16, 22, 27). In Martin and Blady's study, lympho-epitheliomas were grouped under "epidermoid," whereas many investigators, though minimizing the frequency of lympho-epitheliomas, would allot more unproved examples to the lymphosarcoma classification (16). We find that, by including transitional-cell carcinoma in the epidermoid group (57.5 per cent of the total), the relative number of epidermoid tumors compared to the nonepidermoid agrees well with the figures of Lenz (43 per cent), Kramer (59 per cent), Martin and Blady (59 per cent), Eberhard and Leaming (40 per cent), and Nielsen (43 per cent) (Table VII).

TABLE VII: PATHOLOGY

Classification	University of California Cases	Memorial Hospital Cases	Presbyterian Montefiore Hospitals Cases
Epidermoid carcinoma	14 (17.1%)	17 (19.5%)	27 (43.0%)
Transitional carcinoma	33 (40.3%)	42 (48.3%)	
Lympho-epithelioma	25 (30.5%)	14 (16.1%)	20 (31.7%)
Lymphosarcoma	4 (4.9%)	11 (12.6%)	12 (19.1%)
Adenocarcinoma	2 (2.4%)	3 (3.5%)	3 (4.8%)
Plasmocytoma			1 (1.4%)
Melanocarcinoma	1 (1.2%)		
Miscellaneous sarcoma	3 (3.6%)		
Embryonal	1		
Neurofibrosarcoma	1		
Myxofibrosarcoma	1		
TOTAL	82	87	63

In our series, of the 14 tumors initially causing petrosphenoidal cranial nerve signs or symptoms, 12 were detected on the lateral wall in or near Rosenmüller's fossa, one was a roof lesion, and in another the location was not accurately described. Ten of the 14 were epidermoid-type carcinomas, 5 were lympho-epitheliomas. In this series, we were unable to find any clear-cut correlation between the histology of the tumor and the presence of adenopathy or skull erosion.

TREATMENT AND RESULTS

No overall uniform therapy was instituted in these 82 cases. In general, palpable cervical lymph nodes were treated in addition to the nasopharyngeal area. For the primary tumor external irradiation, intracavitary radium, cobalt 60, or a combination of external and intracavitary irradiation was employed. The cervical node areas, in general, were treated by external irradiation.

Sixteen of the 23 cases without palpable cervical adenopathy received roentgen therapy to the nasopharyngeal area only, and 1, the melanocarcinoma, was treated with intracavitary cobalt 60 alone. In 4 of the patients, cervical lymph nodes later became involved on the same side as the primary lesion, an incidence of 25 per cent, or 1 in 4.

Thirty-one of the 82 patients received 1-Mev external irradiation, either alone or supplemented by intra-oral cone therapy, intracavitary radium, or cobalt 60, to the primary lesion. Irradiation in the medium-volt range was used for the cervical lymph-node areas. The remaining 51 patients were treated at 400 kv, 400 kv with grid, 400 kv with rotation, 200 kv, or 200 kv with grid, any of these modalities being supplemented by intra-oral cone, intracavitary cobalt-60 bead, or intracavitary radium. One patient, who survived thirty-six months, was given 200-kv external irradiation, intracavitary cobalt 60, and intravenous nitrogen mustard.

Intracavitary cobalt 60 was used in 19 patients, according to the technics described by Sooy (28) and Morrison (20). Four of this number were treated solely by intracavitary cobalt to the primary lesion, usually in two applications, for a calculated dose of 6,000 gamma roentgens at the surface of the applicator. The average survival was twenty-five months. One of the 4, a patient with lympho-epithelioma, had a bilateral neck dissection. The remaining 15 patients received external roentgen therapy as well as intracavitary cobalt 60 to the primary site. Six patients

Fig. 2. Nasopharyngeal cancer: survival curve.

survived five years or more; of these, one died with residual or recurrent disease, another is alive, without manifestation of cranial nerve involvement or lymph-node metastasis, ten years after external retreatment with 1 Mev for a recurrent nasopharyngeal lesion. All of the five-year survivors received sufficiently high doses of roentgen therapy to make questionable the actual contribution of the intracavitary irradiation to survival. It should be obvious that the indications for intracavitary irradiation, whether by radium, cobalt 60, or any other radioisotope, are the same, being based on the premise of increasing the dose in the nasopharyngeal cavity when other means are unavailable; they ignore the basic concept of nasopharyngeal irradiation, *i.e.*, delivering a cancerocidal dose of ionizing radiation to both the primary tumor and its adjacent lymphatic drainage areas. Certainly, with supervoltage technics, intracavitary irradiation is not indicated and only increases the danger of radionecrosis. A more detailed analysis of these intracavitary cobalt-60 cases is to be presented at a later date.

In this series, 23 of the 82 patients survived five or more years (28.2 per cent). Seventeen of these 23 were alive in July 1959, without evidence of residual, recurrent, or metastatic disease. One patient is alive but with recurrent disease,

TABLE VIII: FIVE-YEAR SURVIVAL COMPARISONS

Series	Total Number of Patients	Five-Year Survivors
University of California Hospital, San Francisco, Calif.	82	23 (28.2%)
Martin-Blady: Memorial Hospital, New York, N. Y.	87	20 (23.0%)
Kramer: Middlesex, London	54	8 (15.0%)
Lenz: Presbyterian and Montefiore Hospitals, New York, N. Y.	44	13 (29.6%)
Nielsen: Radium Center, Copenhagen, Denmark	77	11 (14.3%)
Smedal-Watson: Lahey Clinic, Boston, Mass.	39	13 (33.3%)

developing eleven years after initial treatment. Six patients of the 18 presently alive have survived more than ten years.

The graph in Figure 2, patterned after Kramer, bears out the general statement that three years post-therapy, a leveling off of mortality occurs. The slope of the line during the first two years following treatment is a disastrously steep one.

The five-year-survival percentage in our institution compares favorably with figures reported by others (Table VIII). Smedal and Watson (27), utilizing supervoltage technics, obtained a 33 per cent five-year survival in 39 patients.

PROGNOSIS AND FACTORS INFLUENCING FIVE-YEAR SURVIVALS

Sex: In this series, the five-year-survival percentage was only slightly higher in females than in males (29.2 and 27.6 per cent, respectively). Martin (16) stated that in most forms of cancer of the upper respiratory and alimentary tracts, especially those treated by irradiation, the prognosis in women is slightly better than in men (Table IX).

Age: In the group under forty years of age, a better five-year survival (50.0 per cent) is noted than in any older age group. McConnell (19), however, in describing 7 young persons (eight to twenty-six years) with nasopharyngeal carcinoma, concluded that the prognosis in this age group is unfavorable. The histologic diagnosis in the youngest patient in our group, a two-year-old girl, was "embryonal sarcoma." The child lived less than a year, although a

TABLE IX: FACTORS INFLUENCING FIVE-YEAR SURVIVAL

	Total Number of Patients	Five-Year Survivals
Sex		
Males	58	16 (27.6%)
Females	24	7 (29.2%)
Age		
Under 40 years	14	7 (50.0%)
40 to 49 years	19	6 (31.6%)
50 to 59 years	27	6 (22.2%)
60 years and over	22	4 (18.2%)
Race		
Caucasian	68	18 (27.5%)
Chinese	14	5 (35.6%)
Cervical adenopathy		
None	23	12 (52.2%)
Unilateral	34	9 (26.4%)
Bilateral	25	2 (8.0%)
Cranial nerve involvement		
On admission	19	1 (5.3%)
Any time	20	1 (5.0%)
Erosion of base of skull	9	0

boy of eleven with an epidermoid carcinoma and bilateral cervical adenopathy treated in 1938 is alive and well today. The oldest patient of our series was seventy-seven and the oldest five-year survivor was seventy-one. One patient, sixty-nine years old, who died of adenocarcinoma of the prostate with bone metastases, was apparently free of his nasopharyngeal disease at the time of death (Table IX).

Race: Five of the 14 Chinese patients surviving more than five years (35.6 per cent) are alive at this time. One of the 5 was treated eleven years ago. Four of the Chinese survivors had transitional-cell carcinoma; the fifth had lympho-epithelioma (Table IX). Eighteen of 68 Caucasians survived five years or more (26.5 per cent).

Cervical Adenopathy: In our series, the patients with no cervical adenopathy had a greater chance of survival of five years or more (52.2 per cent) than those with unilaterally involved cervical lymph nodes (26.4 per cent). There was a depressingly low percentage (8.0 per cent) of survivors among the 25 patients with bilateral cervical adenopathy (Table IX).

Cranial Nerve Involvement: Of the 19 patients with initial detectable cranial nerve involvement, only 1 lived longer than five years. The sole survivor presented with only sixth nerve paralysis (Table IX). According to del Regato, the presence of cranial nerve paralysis does not necessarily indicate a hopeless prognosis, although it is an unfavorable sign. None of the patients with multiple cranial nerve involvement survived five years.

TABLE X: STAGING (GEIST AND PORTMANN) AND PROGNOSIS

	Total Number of Patients	Five-Year Survivals
Stage I: Limited to nasopharynx	16	11 (68.8%)
Stage II: Nasopharynx and palpable cervical nodes	40	11 (27.5%)
Stage III: Nasopharynx, cranial nerves, and/or skull erosion	26	1 (3.9%)

Base of Skull Involvement: Erosion of the skull in 9 patients proved to be a fatal sign. Cranial studies in several of our five-year survivors were reported as suggestive or positive for base-of-skull erosion (Table IX), but years later, when reviewed by other roentgenologists, unaware of the diagnosis or outcome of the cases, these same films were read as negative for erosion.

Staging: Geist and Portmann suggested a clinical staging which would encompass the above signs of cervical adenopathy, cranial nerve paralysis, and skull erosion. In our series, this clinical staging proved to be a valuable hint in the ultimate prognosis. There were over twice as many survivors in Stage I asi n Stage II, and the prognosis in Stage III proved to be as expected (Table X).

Pathology: In this series, as in most others (2, 15, 16, 25), lymphosarcoma appeared to have the best prognosis, although the number of cases reported here is too small to permit definite conclusions. The poor response of the two adenocarcinomas contributes to our belief that this histologic type carries a bad prognosis. This poor prognosis is also seen in other series (15, 16). If these tumors are cylindromatous in nature, total

TABLE XI: PATHOLOGY AND FIVE-YEAR SURVIVALS

Histology	Total Number of Patients	Five-Year Survivals
Epidermoid carcinoma	14	3 (21.4%)
Transitional-cell carcinoma	33	10 (30.3%)
(Total "epidermoid")	(47)	(13) (27.7%)
Lympho-epithelioma	25	6 (24.0%)
Lymphosarcoma	4	3 (75.0%)
Adenocarcinoma	2	0
Melanocarcinoma	1	0
Sarcoma (miscellaneous)		
Embryonal	1	0
Neurofibrosarcoma	1	1
Myxofibrosarcoma	1	0

radioresistance and incurability would not be expected. Again, however, the small number of adenocarcinomas in each series makes dogmatic conclusions hazardous.

The prognosis of the transitional-cell carcinomas and the epidermoid carcinomas does not greatly differ from that of the lympho-epitheliomas. This would tend to support those pathologists who maintain the epidermoid identity of most so-called lympho-epitheliomas. No attempt was made at sharp separation of differentiated from undifferentiated epidermoid carcinoma for statistical purposes, although it is significant that 5 of the 14 epidermoid carcinomas (omitting the transitional-cell carcinomas) were considered to be truly anaplastic. One of the 5 patients with this type of tumor survived five years. Of the remaining 9 with epidermoid carcinoma, 2 survived. If we consider the transitional-cell carcinoma an anaplastic variety of the epidermoid carcinoma, we would agree with Baclesse (2) that the outcome in undifferentiated carcinomas is more favorable than that in differentiated epidermoid carcinoma (Table XI).

SUMMARY

Eighty-two consecutive patients with malignant nasopharyngeal tumors were treated at the University of California, Department of Radiology from 1932 to 1954 (twenty-two years). Of these, 23 (28.2 per cent) survived five years or longer.

Malignant nasopharyngeal neoplasms represented 13.3 per cent of all malignant tumors of the head and neck and 2.4 per cent of all malignant neoplasms treated with irradiation. The incidence was higher (*a*) in men as compared to women, (*b*) in Chinese as compared to Caucasians, and (*c*) in the age group between forty and sixty years.

The disease remained unrecognized by patient and physician for an average of eight months (with a high percentage of patients being treated conservatively or surgically under mistaken diagnosis). Most frequent symptoms and signs were cervical adenopathy, nasal obstruction and bleeding, and deafness. Many patients had involvement of cranial nerves and/or skull erosion at the time of correct diagnosis.

Epidermoid-type tumors occurred in 47 patients. Next in order of frequency were lympho-epitheliomas, lymphosarcomas, adenocarcinomas. Individual cases of melanocarcinoma, embryonal sarcoma, neurofibrosarcoma, and myxofibrosarcoma were also seen.

Treatment, in general, consisted of local irradiation of the nasopharyngeal tumor and immediate lymphatic drainage areas, either by external roentgen therapy alone or combined with intracavitary irradiation, as well as external irradiation to the cervical lymph node areas when nodes were palpable. Sixteen of the 23 patients without palpable cervical adenopathy received no treatment to the cervical node area. In 4 of these 16 patients (25 per cent) cervical adenopathy subsequently developed.

The most favorable prognosis was offered by tumors in patients forty years of age and under, those in Chinese, lymphosarcomas, and lesions of Stage I (Geist and Portmann)—absence of cervical adenopathy, cranial nerve involvement, or skull erosion.

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SUMMARIO IN INTERLINGUA

Maligne Tumores Nasopharyngee: 82 Patientes Consecutive, Tractate in un Periodo de Vinti-Duo Annos

Octanta-duo patientes consecutive con histologicamente verificate tumores nasopharyngee maligne esseva tractate al Universitate California inter 1932 e 1954. Inter istes, 23 (=28,2 pro cento) superviveva cinque annos o plus. Le gruppo total de 82 casos representava 13,4 pro cento del maligne tumores de capite e collo e 2,4 pro cento del maligne tumores de non importa qual sito que esseva tractate durante le mesme periodo. Le incidentia de tumores nasopharyngee esseva plus alte in homines que in feminas, in chineses que in caucasianos, e in le gruppo de etates de inter quaranta e sexanta annos que in alteres.

Le morbo remaneva non-recognoscite per le patiente e le medico durante un

periodo medie de octo menses. Un alte procentage de casos esseva tractate initialmente sub diagnoses erronee. Le plus frequente signos e symptomas esseva adenopathia cervical, obstruction e sanguination nasal, e surditate. Al tempore quando le correcte diagnose esseva establite, multes del patientes habeva affectiones de nervo cranial e/o erosion del cranio.

Tumores de typo epidermoide occurreva in 47 patientes. Sequeva in le ordine del frequentias lympho-epitheliomas, lymphosarcomas, adenocarcinomas. Esseva etiam incontrate casos individual de melanocarcinoma, sarcoma embryonal, neurofibrosarcoma, myxofibrosarcoma.

In lor apparentia macroscopic, tumores del nasopharynge pote esser ulcerate (con location le plus frequentemente in le pariete posterior o basse in le fossas de Rosenmuller), lobulate (con origine, usualmente, in le area del tuba auditive e apparente in le forma de lympho-epithelioma o non-differentiate carcinoma epidermoide), o exophytic non-ulcerate.

Nulle generalmente uniforme therapia esseva instituite in iste 82 casos. Normalmente, palpabile nodos lymphatic del area cervical e etiam le area nasopharynge recipeva irradiation. Irradiation externe, radium intracavitari, cobalt 60, o un combination de irradiation externe e intracavitari esseva applicate al tumor primari. Le areas de nodo cervical esseva generalmente tractate per irradiation externe.

Un gruppation del casos secundo lor stadios clinic con le signos de adenopathia cervical, paralyse de nervo cranial, e erosion del cranio se provava utile ab le puncto de vista del prognose. In le gruppo del Stadio I (con tumores restringite al nasopharynge), le frequentia del superviventes esseva duo vices plus alte que in le gruppo del Stadio II (con tumores in le nasopharynge e palpabile nodos cervical), e le prognose in le gruppo del Stadio III (con affectiones de nervo cranial e/o erosion del cranio) esseva de facto tanto mal como on lo habeva expectate. Le plus favorabile prognose esseva offerite per tumores in patientes de etates de quaranta annos o minus, per tumores in chineses, per lymphosarcomas, e per lesiones de Stadio I (Geist e Portmann) con absentia de adenopathia cervical, de affectiones de nervo cranial, e de erosion del cranio.

Werner's Syndrome: A Clinical-Roentgen Entity[1]

HAROLD G. JACOBSON, M.D., HAROLD RIFKIN, M.D., and DOROTHEA ZUCKER-FRANKLIN, M.D.

In 1904, Otto Werner (1) described a syndrome called "cataract in connection with scleroderma" which involved 2 brothers and 2 sisters in a family of 6 children. Thirty years later, Oppenheimer and Kugel (2) published the first complete report of Werner's syndrome in the American literature, as observed in twin brothers at Montefiore Hospital in New York City. Since then, 64 documented cases of this syndrome have been described (3–19), but for only 2 of these, were there authoritative autopsy observations.

From the published literature Werner's syndrome may best be described as follows: The disease occurs with equal frequency in both males and females and becomes manifest shortly after adolescence. A variety of disturbances are noted at this time, including loss of the subcutaneous tissues and muscle mass of the extremities, progressive changes in the skin of the hands and feet, graying of the hair with premature alopecia, and impairment of normal growth. As the condition progresses, the extremities become increasingly thin, while the trunk becomes disproportionately stocky. Indolent ulcers frequently develop at pressure points in the lower extremities, usually in the region of the heels, toes, and malleoli of the ankles. The skin assumes a scleroderma-like appearance, with hyperkeratosis and atrophy. The hair over the eyebrows, pubis, axillae, and face is thinned and downy in appearance. Complete baldness supervenes at an early age, and the patient generally appears prematurely old. The voice becomes weak and high-pitched and examination may reveal a characteristic vascular web of the vocal cords. There is generalized premature arteriosclerosis, and zones of metastatic calcification are frequently observed in the skin and subcutaneous tissues. The skeleton shows varying degrees of osteoporosis, with osteoarthritis of the peripheral joints and spondylosis deformans. Juvenile cataracts are not unusual. Diabetes is often present. A majority of patients exhibit varying degrees of impotence and sterility. Siblings are frequently affected and *forme fruste* types have been described.

The typical patient shows premature aging, shortness of stature, thin, spindly lower extremities, a large trunk, and facies characterized by beaking of the nose, shallow orbits, and loss of the periorbital connective tissue.

The major pathological findings are related to the extensive arteriosclerotic changes in the coronary and peripheral vessels. The skin lesions, originally thought to be those of scleroderma, simply reflect hypoplastic and atrophic changes. The various endocrine organs which have been etiologically implicated at one time or another show no specific histologic abnormality. A striking finding is the frequent coexistence of neoplastic disease, which includes carcinoma of the breast, fibrosarcoma of the soft tissues, hepatoma, uterine sarcoma, and melanosarcoma of the skin.

The etiology of this syndrome is unknown, although there are scattered reports indicating that endocrine dysfunction may be responsible. However, published data show no definitive findings to support this concept.

We have had the opportunity of studying a total of 9 cases, 6 of which have come to autopsy. The purpose of this paper is to present our findings in this series.

CLINICAL MATERIAL

Eight cases have been collected from the files of the Montefiore Hospital in New York City since the early 1930's.

[1] From the Divisions of Diagnostic Radiology and Medicine, Montefiore Hospital and the Department of Radiology, New York University, College of Medicine, New York, N. Y. Presented at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15–20, 1959.

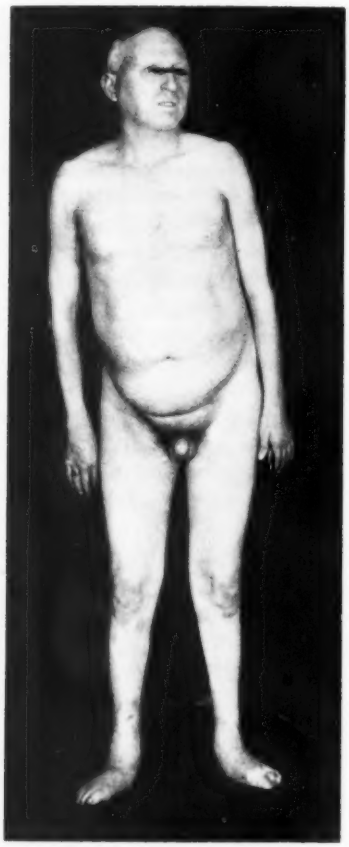


Fig. 1. Case 2. Characteristic facies of a patient with Werner's syndrome (aged 41) are seen. The prominent features include prematurely aged appearance, relatively short stature, baldness, sparse eyebrows, taut skin, leg and feet ulcers, feet deformities, and atrophic genitalia.

Three of these—Cases 1, 2, and 3—have been previously reported (2, 3, 4). The ninth patient, hospitalized elsewhere, was a sibling of one of the Montefiore group (Case 6). Information supplied by this latter patient suggested the possibility of a similar condition in the sibling, and this was subsequently confirmed.

The probable age of onset for manifestations of this syndrome and the age at which the patient was first hospitalized are noted in Table I. A summary of the clinical findings is given in Table II,

TABLE I: WERNER'S SYNDROME: PROBABLE AGE OF ONSET AND FIRST HOSPITAL ADMISSION FOR NINE PATIENTS

Case	Apparent Age (years) at Onset of First Symptoms or Signs	Age (years) on First Hospital Admission
1	15	34
2	17	41
3	23	38
4	35	50
5	37	51
6	28	59
7	20	40
8	18	38
9	Not certain	43

including information concerning race, abnormalities of the eye, hair growth, skin and musculature, the voice, peripheral pulses and heart, family history, ulcerations of extremities, presence of diabetes, status of genitalia and sexual history, abnormal laboratory findings, associated tumors, and other diseases.

Certain findings were uniformly present. All patients were of Jewish descent. (The hospital population at Montefiore Hospital in the years in which most of these cases were accumulated was preponderantly Jewish.) Eye abnormalities occurred in all 9 cases, with cataracts in 8. Abnormalities of hair growth, with early graying, were also seen in all. The skin was invariably taut, shiny, and scleroderma-like, particularly over the extremities, while atrophy of the musculature of the extremities was seen in 7 cases. A positive familial history, in one form or another, was obtained from all patients, 6 of them mentioning early graying of the hair, cataracts, diabetes, etc., in the family background. Two pairs of patients were siblings (Cases 1 and 2; 6 and 9). Ulcerations of the lower extremities, particularly about the bony points (malleoli) were seen in the entire series.

Cardiac abnormalities were found in 8 of the 9 patients. At least 3 died of a myocardial infarct, 5 gave a history of angina and/or myocardial infarct, and in 6 a systolic murmur was heard, either in the apical or aortic region. Abnormally small genitalia or a history of functional

TABLE II: WERNER'S SYNDROME: SUMMARY OF CLINICAL FINDINGS IN NINE PATIENTS

Observation	No. of Patients	Subdivisions*	
Race	9 Jewish		
Eye abnormalities	9	Cataracts	8
		Proptosis or pseudoproptosis	2
		Exophthalmos or pseudoexophthalmos	1
Abnormalities of hair growth	9	Early graying	9
		Early balding	6
Abnormalities of skin and musculature	9	Taut, scleroderma-like skin	9
		Atrophy of musculature of extremities	7
Positive familial history	9	Other familial stigmata (early graying of hair, cataracts, diabetes, etc.)	6
		Consanguinity	2
		Werner's syndrome	1
Ulcerations of extremities	9	Lower extremities	9
		Upper extremities	2
Cardiac abnormalities	8	Systolic murmur (apical or aortic)	6
		Myocardial infarct or angina	5
Absent or diminished peripheral pulses	7	All in lower extremities	
Status of genitalia, sexual history, etc.	7	Small genitalia	4
		Abnormal menstrual history	2
		Diminished or absent libido	1
Voice abnormalities	6	High-pitched	4
		Husky	2
		Low-pitched	1
Diabetes	6		
Abnormal laboratory findings (except findings seen in diabetics)	6	Blood calcium elevation	2
		Uric acid elevation	2
		Blood cholesterol elevation	2
Associated tumors	3	Hepatoma	1
		Fibroliposarcoma, forearm	1
		Osteogenic sarcoma, orbit	1
		Meningioma	1 †
		Thyroid adenoma	1
Other associated diseases	2	Hyperthyroidism	1
		Gout	1
Course		Dead	7
		Living	2

* Multiple findings in some patients. † Same patient.

hypogonadism was noted in 7 cases. Diabetes occurred in 6. Six patients had voice abnormalities, with a high-pitched voice in 4. An elevated blood calcium in 2 patients and uric acid elevation in 2 others are of indeterminate significance, although full-blown clinical gout developed in 1 instance, at the age of thirty-two (Case 9).

The presence of malignant tumors in 3 of the series is of interest—hepatoma, fibroliposarcoma of the soft tissues, and osteogenic sarcoma of the orbit. The orbital tumor was found at autopsy to be associated with multiple intracranial meningiomas. In Case 6 there were symptoms of gastric outlet obstruction with a hypoplastic pyloroduodenal segment which ultimately caused the patient's death, following exploratory laparotomy. Chronic cicatrizing peptic ulcer had been suspected rather than the apparently anomalous hypoplasia found on exploration. Seven patients are dead at the time of this presentation; 2 are still living.

The typical patient with Werner's syndrome, based on our material (Fig. 1), is of Jewish descent with a history of diabetes and a strong familial tendency to the disease. There is a history of premature graying of the hair and alopecia, and cataract formation starts at an early age. The individual is generally quite small in stature and appears prematurely old, with beaking of the nose and proptosis of the eyes. The genitalia may be small, with some gonadal malfunction. The skin is scleroderma-like in appearance, while the musculature of the extremities is quite atrophic. The voice is frequently high-

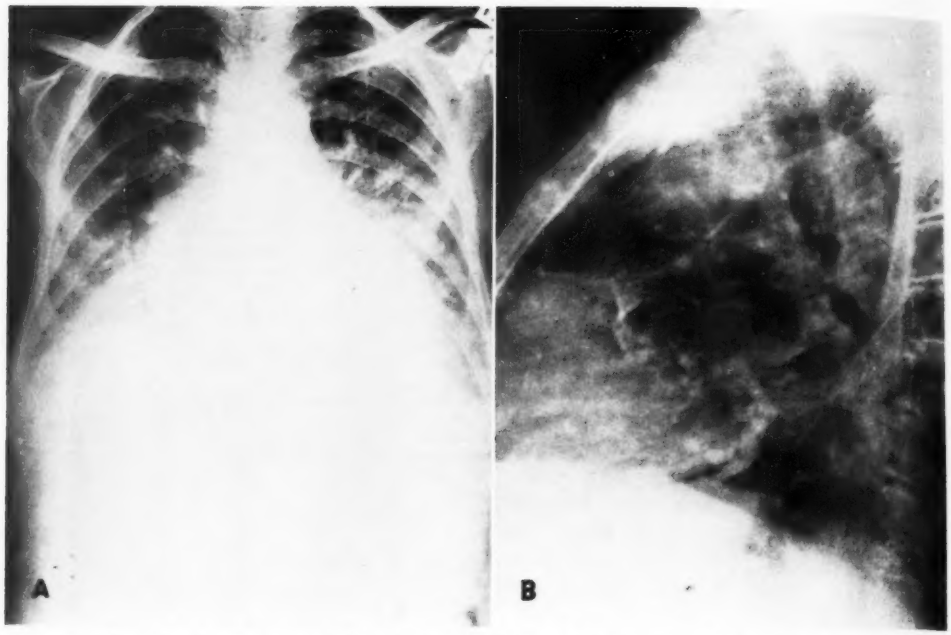


Fig. 2. Case 4. A. Postero-anterior chest roentgenogram shows generalized cardiac enlargement with pulmonary congestion.

B. Lateral chest roentgenogram shows calcification in mitral and aortic valves, with faint calcific deposits in coronary arteries. Wall of ascending aorta also calcified. Moderate degree of spondylosis deformans in dorsal spine.

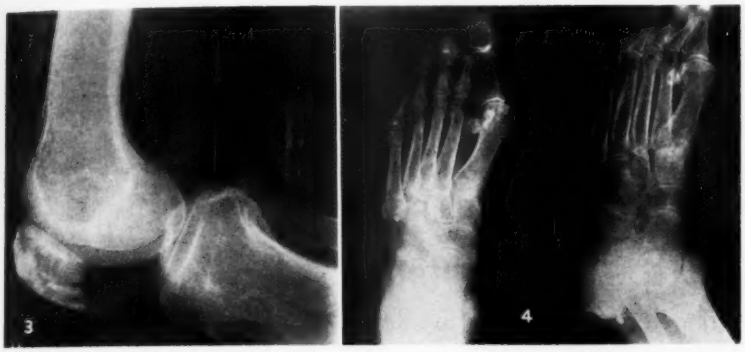
TABLE III: SUMMARY OF ROENTGEN FINDINGS

Observation	No. of Patients	Subdivisions*	
Osteoporosis	9	Considerable in hands and feet	9
		Generalized	8
Soft-tissue atrophy of extremities	9	Lower extremities	9
		Upper extremities	8
Soft-tissue calcification in extremities	9	Ankles	8
		Feet	6
		Hands	5
		Knees	3
		Elbows	2
		Shoulders	1
Peripheral vascular calcification	7	Generalized, including carotid siphon	4
Osteoarthritis and/or spondylosis deformans	7	Osteoarthritis of peripheral joints	6
		Spondylosis deformans	5
Gross foot deformities	7	Extension and flexion deformities	6
		Hallux valgus	3
		Pes planus	3
		Bizarre (not classified)	2
Neurotrophic bone changes in feet	7		
Abnormal skeletal habitus (small bones)	7		
Osteomyelitis	7	Feet	7
		Ankles and leg bones	5
		Hands	2
		Wrists and forearm bones	2
Cardiac abnormalities	3	Calcification of mitral valve or annulus	3
		Calcification of coronary arteries	3
		Calcification of aortic valve	2
		Enlarged heart	2
Other significant roentgen features	5	Infectious arthritis	4
		Hypoplastic pylorus and duodenum	1
		Atrophic pyelonephritis	1

* Multiple findings in some patients.

pitched. The peripheral pulses of the lower extremities are diminished or absent, and superficial ulcerations, particularly over the bony prominences of the lower extemities, are common. The patient frequently gives a story of angina or myocardial infarct, and systolic murmurs are often heard over the apical or aortic areas. The development of a neoplasm is not uncommon.

Osteoporosis, soft-tissue atrophy of the extremities, and heterotopic calcifications in the soft tissues of the extremities were seen in all 9 patients. The osteoporosis and soft-tissue atrophy were most marked in the hands and feet. The soft-tissue calcifications often corresponded with the ulcerations seen clinically and were most prominent about the bony malleoli, particularly about the ankles. It may be



Figs. 3 and 4. Case 4. The right knee (lateral view) shows considerable lime deposition in the patellar tendon and in anterior soft tissues of lower thigh. Calcification is seen in popliteal artery.

The left foot shows bone and soft-tissue atrophy, calcifications in the soft tissues about the ankle, the lower leg, and in the first and fifth toes, neurotrophic and/or osteomyelitic changes in the second, fourth, and fifth toes, and arterial calcification.

ROENTGEN FINDINGS

The roentgenograms on 6 of the patients were available for review. The films on Cases 1, 2, and 3 unfortunately were lost or destroyed (these examinations were performed over twenty years ago), but they could be evaluated from comprehensive roentgenographic reports available in the hospital charts. The significant roentgen findings in all the cases include osteoporosis, small bone stature, soft-tissue atrophy of the extremities, peripheral arterial calcification, metastatic calcification of soft tissues, neurotrophic changes in the bones of the feet, gross foot deformities, osteomyelitic and/or osteomyelitic-like lesions of the extremities, osteoarthritis of the peripheral joints and spondylosis deformans, and abnormal cardiac findings, including heart enlargement, valve calcifications, and coronary artery calcifications. These findings are summarized in Table III.

that the soft-tissue calcifications, which in several instances were quite superficially placed, predispose to the development of superficial skin and subcutaneous ulcerations. Peripheral vascular calcification (arterial) was seen in 7 cases.

Neurotrophic bone changes, all in the feet, were noted in 7 patients. The characteristic findings were marked "spindling," thinning and narrowing of the terminal tufts, much like the changes frequently noted in diabetics with superficial ulcerations. Since ulcerations were present in all of these patients, the two may very well be related.

A notable feature of our series, and one not specifically described or emphasized in the literature, is the occurrence of osteomyelitis or lesions resembling osteomyelitis in 7 of the 9 cases. These were observed most commonly in the feet, ankles, and leg bones, but were in addition to the neurotrophic changes in the terminal tufts

of the feet. Usually, these lesions were characterized by destructive changes, with definite lytic areas; one example each of sequestration and periosteal cloaking was encountered. The frank osteomyelitic-like lesions and the neurotrophic bone-end changes in the feet may well be related. In 4 patients, infectious arthritis was seen, probably secondary to osteomyelitis. It is our feeling that the osteomyelitis is associated both with the metastatic calcification in the soft tissues and with generalized cardiac enlargement. These were demonstrated on the chest roentgenograms of 3 patients.

The operative finding in Case 6 of a hypoplastic pylorus and duodenum after development of gastric outlet obstruction is of interest as an associated congenital anomaly. An atrophic pyelonephritis seen in Case 7 could be an incidental finding.

The roentgen findings are illustrated in Figures 2 to 21.

In summary, a typical patient with

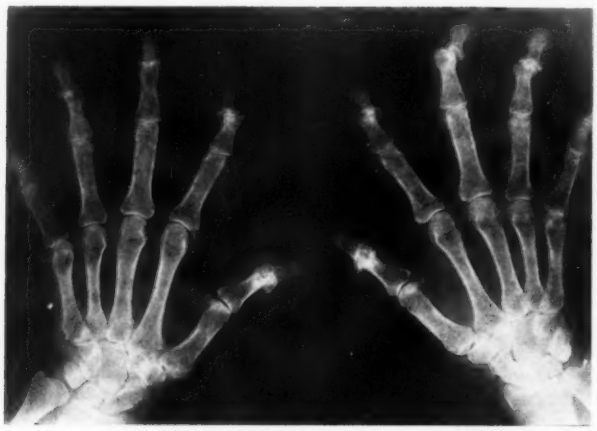
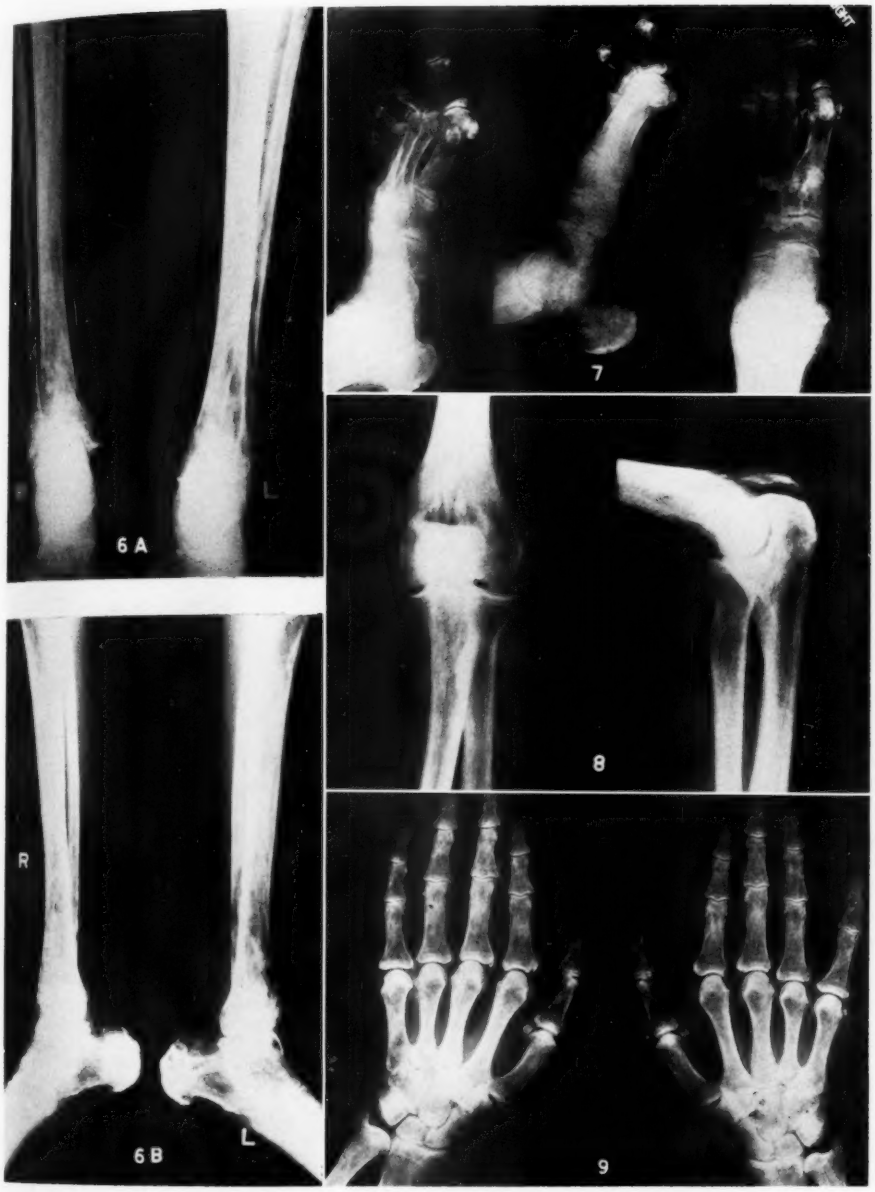


Fig. 5. Case 4. The hands show extensive bone and soft-tissue atrophy with marked osteoarthritic changes, particularly involving the distal interphalangeal joints, with subluxations. Soft-tissue calcification is seen in the left index finger.

the ulcerations of the extremities, in part secondary to the advanced arteriosclerosis and diabetes.

The texture and appearance of the bony skeleton were those of a generally small individual in 7 of the 9 patients. Gross foot deformities were seen in 7 of the series, with severe extension and flexion deformities of the toes being most common. In 2 instances, the foot deformities were so bizarre that they could not be classified. Osteoarthritis of the peripheral joints was noted in 6 cases and spondylosis deformans involving the dorsal and lumbar spine in 5.

The most notable cardiac abnormalities were calcification of the mitral and aortic valves and coronary arteries, as well as Werner's syndrome *roentgenographically* will show generalized osteoporosis, more extensive in the hands and feet, with all the bones small in stature; soft-tissue atrophy of the upper and lower extremities; heterotopic soft-tissue calcification, mostly in the lower extremities and about the bony prominences of the ankle; extensive peripheral vascular calcification, particularly in the extremities; osteoarthritis of the peripheral joints and spondylosis deformans; neurotrophic bone changes of the feet, gross foot deformities, and frank osteomyelitis, particularly in the bones of the feet. Heart abnormalities, including an enlarged heart with failure, calcified coronary arteries, and valvular calcifications, are not infrequent.



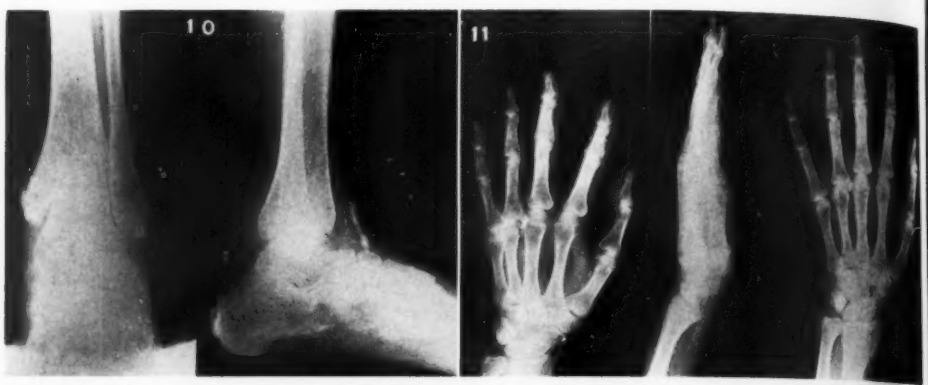
Figs. 6–9. Case 5.

Figs. 6, A and B. Marked bone and soft-tissue atrophy of the lower extremities with calcifications in soft tissues. Arterial calcification is also present.

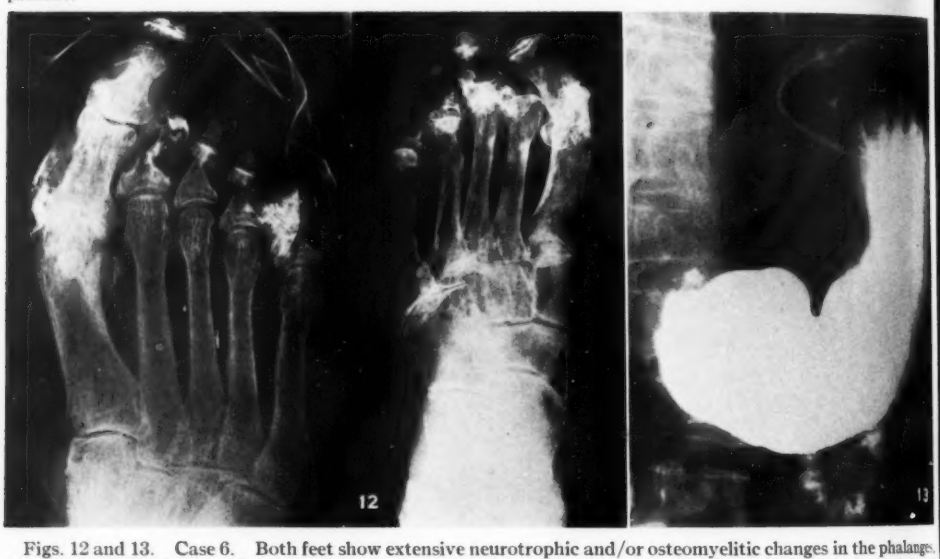
Fig. 7. The right foot shows extensive atrophy with calcification in soft tissue about os calcis and medial malleolar tip. Neurotrophic and/or osteomyelitic changes in tip of terminal phalanx of fifth toe (not too well delineated).

Fig. 8. The left elbow shows extensive soft-tissue calcifications (tendinous) adjacent to medial humeral epicondyle and just above the olecranon. Osteoporosis is present.

Fig. 9. The hands show considerable bone and soft-tissue atrophy, with soft-tissue calcifications at several sites in joint regions. Arterial vascular calcification also noted.



Figs. 10 and 11. Case 6. The right ankle (Fig. 10) shows extensive bone and soft-tissue atrophy, soft-tissue calcifications at characteristic sites, and marked arterial calcification. The left hand (Fig. 11) shows the typical para-articular and arterial calcifications, as well as marked bone and soft-tissue atrophy. Osteoarthritis is also present.

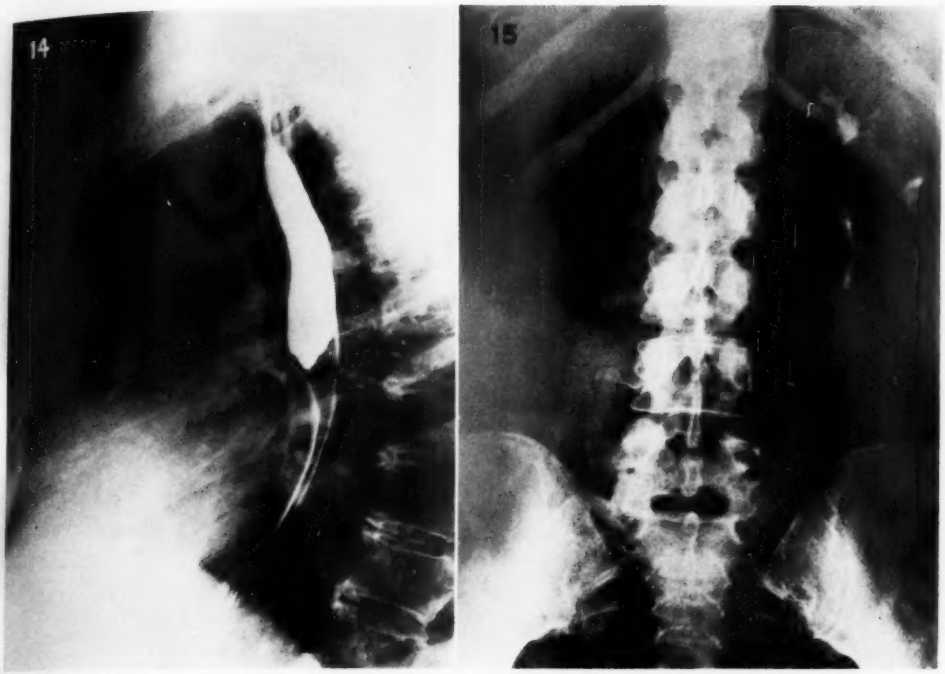


Figs. 12 and 13. Case 6. Both feet show extensive neurotrophic and/or osteomyelitic changes in the phalanges, with considerable bone and soft-tissue atrophy. Old infectious arthritis of the left first toe at the metatarsophalangeal joint is noted. There are soft-tissue calcifications about the medial malleolus of the left ankle, with arterial calcification. Dressings at sites of superficial ulcerations are seen, with opaque medication.

A right anterior oblique roentgenogram of the barium-filled stomach shows the incomplete outlet obstruction due to a hypoplastic pylorus and duodenum.

PATHOLOGIC FINDINGS

Six patients came to autopsy, and in a seventh a skin biopsy was reported as unremarkable. Nothing significant was found to add to the information obtained clinically and roentgenologically. A summary of the pathologic findings is given in Table IV. The generalized arteriosclerosis seen in all instances, the heart abnormalities in 5 of the 6 autopsied cases, and the testicular atrophy were all noted clinically. The microscopic findings in the skin and subcutis were not unexpected; atrophy of the epidermis was seen 4 times, atrophy of the rete pegs twice, and thickening of the corium with fibrous tissue twice (Fig. 22). The relatively high incidence of tumors was confirmed in the autopsy series. None of these findings is contributory to an understanding of the cause of this syndrome.



Figs. 14 and 15. Case 7. A left lateral chest roentgenogram (Fig. 14) with barium-opacified esophagus shows evidence of left atrial enlargement. The mitral valve is calcified and linear calcifications are seen in the coronary arteries. Note the moderately advanced spondylosis deformans in the dorsal spine.

Roentgenogram of the upper abdomen (Fig. 15) during intravenous urography shows no opacification on the right, with a small kidney outline (atrophic pyelonephritis). Extensive renal-artery calcifications are noted bilaterally, as well as calcification in the abdominal aorta and iliac arteries.

TABLE IV: SUMMARY OF PATHOLOGICAL FINDINGS (6 AUTOPSIES, 1 SKIN BIOPSY)

Observation	No. of Patients	Subdivisions*	
Generalized arteriosclerosis	6	Heart abnormalities (calcification of coronary arteries, myocardial infarct or fibrosis, valve calcifications)	5
Microscopic changes in skin	5	Atrophy of epidermis	4
		Thickening of corium with fibrous tissue	2
		Atrophy of rete pegs	2
Neoplastic disease	3	Hepatoma	1
		Fibrosarcoma	1
		Multiple intracranial meningiomas	1 †
		Thyroid adenoma	1 †
Testicular atrophy	3		

* Multiple findings in some patients.
† Same patient.

DIFFERENTIAL DIAGNOSIS

A number of conditions may at times be confused with Werner's syndrome. These include, among others, hyperparathyroidism, arteriosclerosis with diabetes, Simmonds' cachexia due to pituitary hypofunction, scleroderma, diffuse metastatic calcinosis of unknown cause, hypervitaminosis-D, sarcoid, renal and/or gastrointestinal osteomalacia, Cushing's syndrome, hyperthyroidism, poliomyelitis with calcification, Rothmund's syndrome, neurodermatitis with cataract (cataracta dermatogenes), dystrophia myotonica, progeria with nanism (Hutchinson-Gilford's syndrome), and anhydrotic ectodermal dysplasia. Of these, the most important, from the point of view of possible confusion

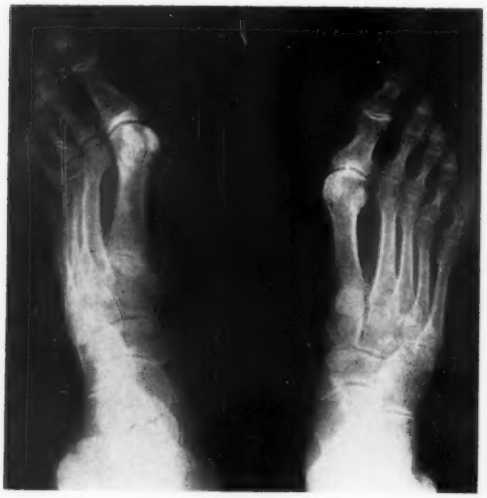


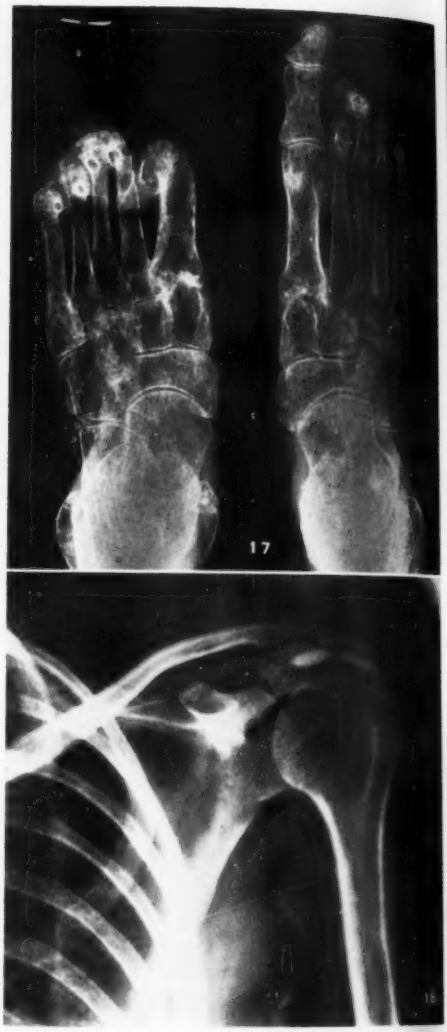
Fig. 16. Case 7. Bone and soft-tissue atrophy in the feet, calcifications in soft tissues, and arterial calcification. There is a postural deformity of the left foot, with "spindling" of the terminal tufts of a number of toes of both feet.

with Werner's syndrome, are the following:

Scleroderma: Here the skin changes are apparently indistinguishable from those seen in Werner's syndrome, but the hair and eye abnormalities, the ulcerations in the extremities, and the multiple osteomyelitic-like lesions are not generally observed. The roentgen changes in the gastrointestinal tract in scleroderma are not found in Werner's syndrome, nor are the pulmonary fibrotic manifestations.

Hyperparathyroidism: None of the clinical stigmata found in Werner's syndrome is seen in hyperparathyroidism, although bone atrophy and arterial and soft-tissue calcifications are common. While there was a mild elevation of the serum blood calcium in 2 of our patients, the laboratory findings in hyperparathyroidism are usually specific.

Arteriosclerosis and Diabetes: Neurotrophic and/or osteomyelitic changes in the extremities, as well as the arteriosclerosis and heart complications seen in Werner's syndrome, may be found in any patient with generalized arteriosclerosis with or without diabetes. The other clinical features, however, including the skin changes,



Figs. 17 and 18. Case 8. A postero-anterior roentgenogram of both feet (Fig. 17) shows bizarre deformities of the toes of the right foot with subluxation of the second toe and extensive flexion and extension deformities. Deformities are less marked in the left foot, with a subluxation in the second toe. Soft-tissue calcifications about the malleoli of the ankles are noted, with extensive bone and soft-tissue atrophy present.

A postero-anterior view of the left shoulder (Fig. 18) shows extensive lime deposition above the humeral head. Bone and soft-tissue atrophy are quite evident.

and eye and hair abnormalities, are not seen in such patients.

Rothmund's syndrome is also a heredofamilial disease associated with cataracts and usually mild aberrations of sexual

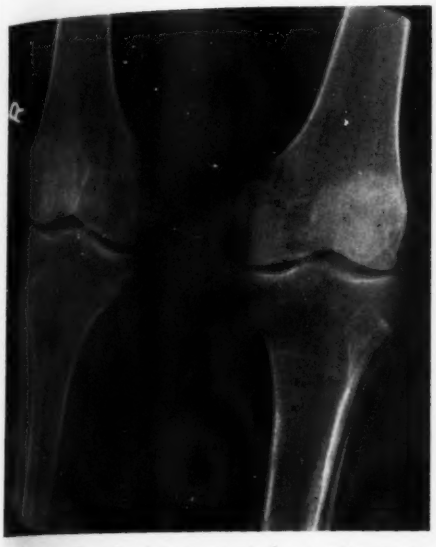


Fig. 19. Case 9. A postero-anterior roentgenogram of both knees shows considerable bone and soft-tissue atrophy. A lytic area is seen in the medial aspect of the upper right tibial shaft, with less clearly defined but similar zones involving the same area on the opposite tibia. These lytic areas have the appearance of osteomyelitic foci.

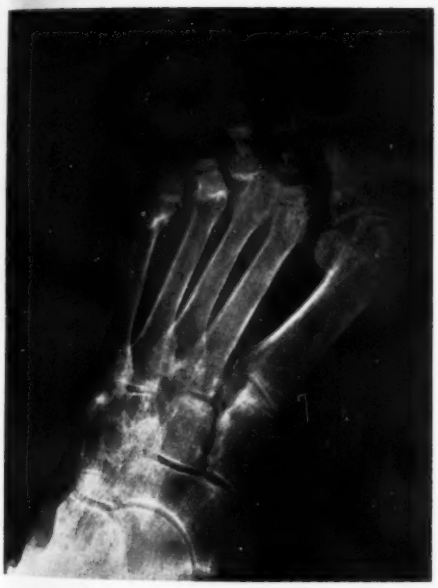


Fig. 20. Case 9. Postero-anterior roentgenogram of the left foot shows extensive bone and soft-tissue atrophy, with a marked metatarsus primus varus, hallux valgus deformity. Suppurative arthritic changes secondary to osteomyelitic lesions are seen involving the metatarsophalangeal joints of the second and fifth toes, with subluxations at the third and fourth toes.

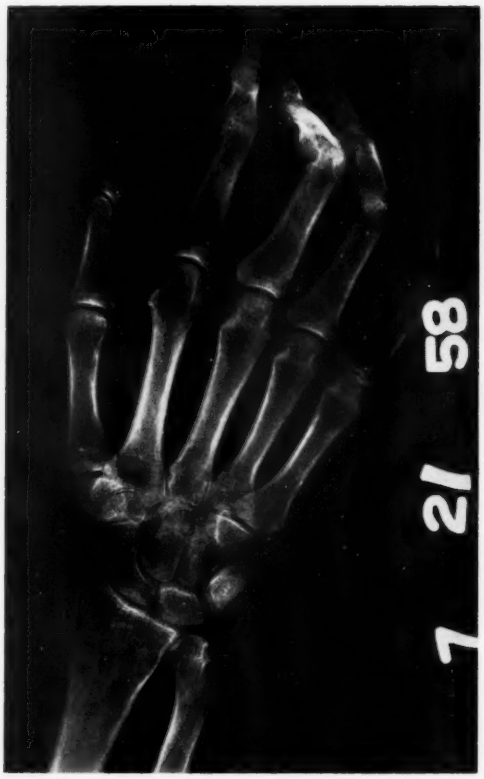


Fig. 21. Case 9. The right hand shows an osteomyelitic-like focus involving the ulnar styloid, with adjacent soft-tissue swelling. A lytic area is seen in the head of the proximal phalanx of the third finger. Extensive atrophy of bone and soft tissue are present.

development, but no retardation of growth. Ulcers are seldom found, and there is usually no arteriosclerosis, osteoporosis, canities, or atrophy of the soft tissues of the extremities. The skin changes that may be present in Rothmund's syndrome are unlike those seen in Werner's syndrome even though the skin may be atrophic and thin.

Cataracta Dermatogenes: In this disease, cortical subcapsular opacities begin some years after the onset of childhood eczema with a heredofamilial history. Cataracts are relatively infrequent. Thickening of the skin associated with asthma is frequently noted in young persons who are emotionally labile. The skin involvement has a characteristic distribution. The osteomyelitic and/or neurotrophic bone

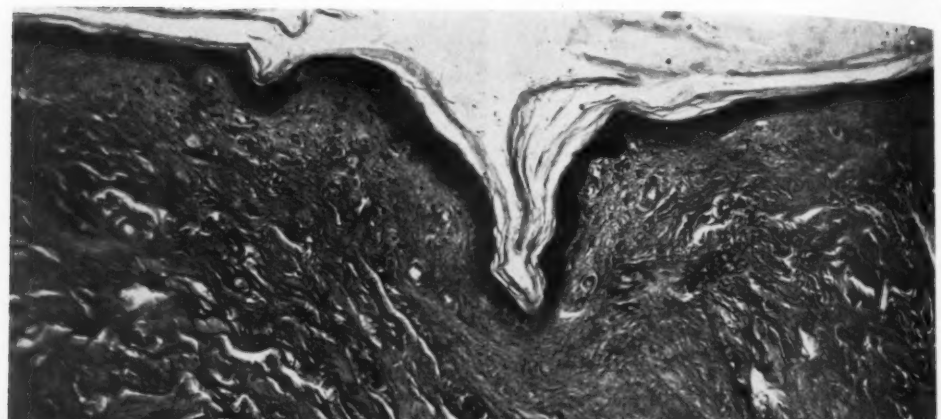


Fig. 22. Case 6. Photomicrograph (×110) demonstrating atrophy of the rete pegs and fibrous connective-tissue thickening of the corium.

changes found in Werner's syndrome are not seen.

Dystrophia myotonica is another familial disorder characterized by wasting of the striated muscle groups, with frequent cataracts, baldness, and testicular atrophy. Infertility and menstrual irregularities have also been reported, and diabetes may occasionally be present. Cardiac involvement is not uncommon, with generalized heart enlargement, congestive failure, hypotension, and conduction defects in the electrocardiogram being frequently present. There is some resemblance to Werner's syndrome, but enough differential points exist so that confusion should not be too great.

Progeria with nanism (*Hutchinson-Gilford's syndrome*) comprises dwarfism, total alopecia, atrophic skin, and premature senility in patients in whom cataracts and cutaneous ulcers do not develop and who give no familial history as in Werner's syndrome. The progeria in Hutchinson-Gilford's syndrome develops in early childhood, whereas in Werner's syndrome the aging usually begins in the second decade.

Anhidrotic ectodermal dysplasia is a hereditary disorder, predominant in males, with anhidrosis, abnormalities in dentition, sparse, dry hair of the scalp, diminished lacrimation, mental retardation, and absence of mammary glands. There are no cataracts, and no senility or premature arteriosclerosis is noted.

Some of the other diseases mentioned may show certain features seen in Werner's syndrome, but the overall roentgen and clinical findings in a case of Werner's syndrome, together with the history, should leave little doubt about the diagnosis in any characteristic case.

SUMMARY AND CONCLUSIONS

We have presented the clinical and roentgen data in 9 cases of Werner's

syndrome, 3 of which have been previously reported.

The clinical and roentgen findings in the usual case of Werner's syndrome are so characteristic that the clinician and radiologist should have no difficulty in making the diagnosis even though certain entities, such as scleroderma, may at times be confusing.

Of our 9 patients, 6 came to autopsy. None of the pathologic data obtained contributes significantly to an understanding of the cause of the disease.

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SUMMARIO IN INTERLINGUA

Le Syndrome de Werner: Un Entitate Clinico-Roentgenologic

Es presentate le datos clinic e roentgenologic de 9 casos de syndrome de Werner. Usualmente le constatationes in casos de iste syndrome es si characteristic que le clinico e le radiologo non pote haber ulle difficultate a establir le diagnose. Le syndrome es characterisate per senilitate prematur, anormalitates del capillatura, formation de cataractas, atrophia del pelle e del musculatura in le extremitates, atrophia del genitales, precoce e progressive arteriosclerosis, e varie anormalitates cardiac, incluse morbo de arteria coronari. Diabete es frequente.

Le significative constatationes roentgenologic include osteoporosis, reducite statura ossee, atrophia de tissu molle in le extremitates, calcification del vasculatura peripheric, metastatic calcification de tissu molle, alterationes neurotrophic in le ossos del pedes, grossier deformitates del pedes, lesiones osteomyelitic e/o osteomyelitoide in le extremitates, osteoarthritis del articulationes peripheric e spondylosis deformante, e anormalitates del constatationes cardiac, incluse allargamento del corde, calcification valvular, e calcification de arteria coronari.

Present Health of Children Given X-Ray Treatment to the Anterior Mediastinum in Infancy[1]

EUGENE A. CONTI, M.D., GEORGE D. PATTON, M.S., M.D., JANE E. CONTI, B.A., and LOUIS H. HEMPELMANN, M.D.[2]

A RECENT SURVEY showed that the incidence of neoplasia in a group of children who had been treated with x-rays in infancy for enlargement of the thymus gland was higher than that in either their untreated siblings or in children of the same age in the population at large (1, 2). In particular, the number of cases of leukemia and thyroid cancer in the irradiated children far exceeded the number expected in a normal group of comparable size and age distribution. Although the findings are consistent with reports of an increased incidence of malignant disease, especially leukemia, in other human populations exposed to ionizing radiation (3–7), certain features of this study are sufficiently unusual to deserve further investigation. First, the doses of radiation were smaller than those formerly believed to be carcinogenic. Second, whereas the thyroid neoplasia and other cancers were found only in children exposed to comparatively high doses of x-rays (more than 200 r), leukemia sometimes occurred in children receiving less than 200 r. Third, because almost all children were selected for treatment on the basis of a diagnosis of thymic enlargement, it is impossible to differentiate the role of this factor from that of irradiation in the development of leukemia and other malignant diseases.

The purpose of the present study is to obtain further information concerning the incidence of malignant disease in children treated with x-rays. The irradiated children in the series to be reported are of particular interest in that most of them had thymus glands of normal size. In this respect, they differ from the children in the survey previously mentioned and in others now being conducted in this country.

TABLE I: DISTRIBUTION OF X-RAY DOSES AMONG CASES

Dose in Air → (r)	75–100	101–200	201–300	301–450	Total
Enlarged thymus	3	43	62	116	224
Normal thymus	67	1,273	0	0	1,340
TOTAL CASES	70	1,316	62	116	1,564

METHODS AND MATERIALS

A survey similar to that described by Simpson and Hempelmann (2) was conducted on a series of 1,564 children in Pittsburgh, who had received x-ray treatments to the thymus gland between 1938 and 1946. The children selected for this survey were included in a previous study of 7,391 surviving full-term children[3] born consecutively in the Pittsburgh Hospital and examined roentgenologically to determine whether or not the thymus gland was enlarged (8). The diagnosis of thymic enlargement, based on roentgenograms, fluoroscopic examination, or both, was made in 224 children, or approximately in 3 per cent of the entire group. Although these children were usually asymptomatic, 80 per cent were treated with 200 to 450 r to the anterior mediastinum. In the course of the study, it was noted that signs and symptoms attributed to thymic enlargement never occurred in treated children who had enlarged thymus glands at birth. Since upper respiratory infections also seemed to be less prevalent in the treated children, it was decided to give all

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[3] The ratio of white to nonwhite children is 23 to 1.

children born between June 1944 and May 1946 small doses of x-rays to the manubrial region. Ninety-five per cent of the 1,340 children so treated were given 150 r and the remainder received 75 to 100 r (Table I). A survey of these children, conducted by mail in 1948, reaching about half the total number, showed no apparent increase in either morbidity or mortality.

The radiation factors used in treatment were: 140 kvp; filtration, 3 mm. Al; skin-target distance, 8 to 9 in.; port size, 4 × 4 cm.; port position, over the manubrium. Increments of 75–150 r were usually given at one- to two-day intervals. All children were treated within seven days after birth; children with illnesses not usually ascribed to thymic enlargement were excluded from the series.

The method of interviewing parents of the treated children was the same as that used by Simpson and Hempelmann (2) except that the telephone was used wherever possible. The families (usually the mother) of the 89.6 per cent of children located were questioned about the present health of the child and serious illnesses in the past. The same information was obtained for 2,923 untreated siblings. Since the mothers volunteered information about the siblings without giving previous thought to the subject, it is possible that information about some dead siblings was missed. If the treated child or sibling was said to be in good health, no further investigation was made. However, if the child had been seriously ill or had died, information was obtained as to the nature and date of the illness, the place of hospitalization, and the names of the attending physicians. The death records of the Pennsylvania State Department of Health were searched exhaustively for all but 15 of the 163 untraced children in the treated series.[4] In addition, the leukemia records of the Health Department were reviewed for the period, 1954–1957.

[4] The death records in the Pennsylvania State Department of Health were checked by clerks from the office of Dr. A. G. Gilliam. This proved to be a time-consuming and usually fruitless task. Time did not permit a thorough search for 15 children.

TABLE II: CASES OF NEOPLASIA OBSERVED IN TREATED CHILDREN AND SIBLINGS

Treated (1564)	Siblings* (2923)
1 osteochondroma†	1 leukemia
	1 lymphosarcoma (? leukemia)
	1 malignant lymphoma
	1 cerebellar tumor
	1 osteoid osteoma†

* A sibling who received x-ray treatment for thymic enlargement at another hospital died of leukemia. This child is excluded from our study.
† Benign tumor.

In tabulating the results, any sibling known to have received or suspected of having received x-ray treatments for any cause was excluded from the study. Nineteen treated children (16 of whom had thymus glands of normal size at birth) were not considered, since they were given further x-ray therapy for thymic enlargement elsewhere.

RESULTS

Table II lists the cases of neoplasia occurring in the treated children and in their untreated brothers and sisters as determined in 1956–58. No cases of leukemia were found in the treated group, whereas 1 untreated sibling died of leukemia and 2 others died of lymphoma. A second child in the group of untreated siblings died of leukemia but was excluded because of treatment with x-rays at another hospital. A sister of one of the treated children had a teratoma at birth; since she was said to have been given x-ray treatment elsewhere, she was excluded from the group of siblings.

Table III shows the numbers of observed and expected cases of neoplasia of all types, as well as of leukemia and thyroid tumors, in the treated children and their untreated siblings. The number of cases of cancer expected to occur in these two series was calculated from the so-called years-at-risk in each age group and cancer rates for the respective age groups taken from a study in 1948 of the cancer incidence in ten American cities (9), one of which was Pittsburgh (10). The observed number of cases of all cancers and of leukemia in the

TABLE III: EXPECTED AND OBSERVED FREQUENCY OF MALIGNANT DISEASE

	Treated Children* (1564)		Untreated Siblings† (2923)	
	Expected†	Observed	Expected‡	Observed
All cancers	(2.52) 4.28	0	(4.03) 5.92	4
Leukemia	(0.51) 0.95	0	(0.91) 1.62	1
Thyroid	(0) 0.03	0	(0) 0.07	0

* The 163 untraced children are assumed to have no cases of malignant disease.

† Siblings are dropped from the study at the age of 20.

‡ The parenthetical values were obtained by use of age-specific cancer rates for Pittsburgh in 1948 (10), whereas nonparenthetical numbers are based on the ten-city survey (9). Since the rate for cancer and leukemia is based on a small number of cases in the Pittsburgh series, it seems preferable to base the expected number of cases on the rate in 10 cities (10).

TABLE IV: EXPECTED AND OBSERVED FREQUENCY OF DEATH

Age	Treated Children (1564)		Untreated Siblings (2923)	
	Expected	Observed	Expected	Observed
Under 1 year	68.7	13*	101.5	56†
1–19 years	17.1	8	30.8	25

* Significance of the difference of this figure from that expected and from that observed in siblings was not tested because of exclusion of obviously ill newborn infants from this series.

† Observed frequency lower than that expected at the 5 per cent level of significance.

sibling group is slightly lower than that expected, but not significantly so. In the treated group, no cases of cancer were found, whereas 2.52–4.28 were expected, and the expected case of leukemia was not observed. It is quite possible that 1 or possibly even 2 cases of cancer or leukemia could have occurred in the 10 per cent of untraced children and might, therefore, have been missed despite all efforts to check the death records. Assuming a random distribution of neoplastic disease between the 90 per cent traced and the 10 per cent untraced children, the chance of all 4 expected cases occurring in the latter group is about 1 in 1,000. If one assumes that no cases of cancer were overlooked in the total series, *i.e.*, no cases occurred when 4 were expected, this could be due to chance less than once in 50 times. One can apply the same reasoning to the frequency of leukemia. Although the 1 expected case of leukemia could easily be overlooked on a chance basis, an increased number of cases of leukemia, say 4 or more, would be missed by chance once in 50 times. As far as the data at hand can be considered valid, there is no positive evidence either for an increased cancer rate or for a greatly increased leukemia rate (4 times expected or more) in the group of children treated by x-rays.

By use of the years-at-risk and age-specific mortality rates for the country at large (11), the expected mortality can be calculated for each group of children. The expected and observed deaths are shown in Table IV and the significance of the differences between comparable frequencies is given. That the observed deaths in the untreated siblings are significantly lower than those calculated from the mortality rates of the entire country is not surprising, since the senior author has previously observed (12) that the fetal loss at the Pittsburgh Hospital is a little more than half that for the population in Pennsylvania or in the U. S. Registration Area. The death rate of the treated children under one year is not meaningful, because only surviving full-term babies discharged from the hospital are included in the study. The difference in observed and expected deaths of the treated children is significant at the 5 per cent level, whereas that in the untreated sibling group is not significant. The death frequency of treated children and that of siblings are not significantly different.

DISCUSSION

It is obvious that the conclusions which can be drawn from a negative study such as this are limited by the size of the population studied, the small number of cases of neoplasia expected, the failure to locate all treated children, and the inability to test negative information. Nevertheless, this is such a unique group that the data obtained must be examined carefully and their validity tested as far as possible. The findings can then be compared to those of other studies with positive conclusions, *i.e.*, a high cancer rate following irradiation in childhood. Ultimately, these data must be pooled with those of

other surveys now under way, to build up a large enough population of children irradiated under different conditions and with varying radiation factors to permit definitive conclusions to be drawn as to the association of irradiation and cancer.

Let us first consider the validity of the data obtained. In an interview study of this type, positive information from the parents about the child's health can usually be confirmed by medical records or death certificates; however, negative information cannot be tested adequately. Thus, a bias is introduced in favor of negative information, and this influences any conclusions about incidence of malignant disease in this group. In particular, instances of malignant disease could have been missed because the parents were not asked about it directly. This is more serious in the case of neoplastic disease with a long life expectancy, such as thyroid cancer, in living children than it is in leukemia or other rapidly fatal malignant conditions. The latter cases would probably have been detected when the death certificates were checked. In addition to the bias inherent in this study, there is an uncertainty factor affecting the validity of the data due to inaccurate reporting or misdiagnosis. For example, 3 children in the treated group are known to have died after brief febrile illnesses. These deaths could conceivably have been due to overwhelming infection superimposed on undiagnosed acute leukemia, possibly in the aleukemic stage. However, in this age of antibiotics, it seems likely that leukemia is only rarely unrecognized—or unsuspected—at some stage of the illness.

A final point influencing the conclusions which can be drawn from this study is the selection of information attributable to failure to locate all patients. Since it is generally accepted that untraceable migratory patients or patients difficult to locate are a selected group, differing in certain characteristics from those patients who are easy to trace, it cannot be assumed that the cases of cancer necessarily are randomly distributed between traced and untraced patients. Thus, cases of malignant disease may have been missed in the untraced group, although the fact that they were not located in the search of death certificates reduces this probability. It should be pointed out that the same bias, uncertainties, and selection encountered in evaluating morbidity of cancer in this series of treated children apply, as well, to the sibling group and to the irradiated children studied in other surveys. These factors become important only when the data obtained by the present method for this group of treated children are compared with vital statistics of the age-specific population at large.

It is possible to compare directly the number of cases of cancer in the treated children and in their untreated siblings without concern for the complication introduced by the failure to locate all treated children. Table III shows that 4 cases of malignant disease occurred in the sibling group of 2,923 children, whereas none occurred in the 1,564 treated children, not a significant difference.

It is germane now to compare the results of this study with those recently compiled by Simpson for the original series of 1,702 children (2) treated for thymic enlargement plus 604 new cases (7). In this total series, 1,070 children were known to have received an x-ray dose of 200 r or less. Three cases of leukemia and 1 thyroid adenoma were found in children receiving 150 r or less and leukemia developed in 1 child who received 200 r. In the present series, no case of malignant disease was found in the 1,564 children, of whom 1,386 received less than 200 r. Therefore, it seems likely that the cancer rate in the present group of children receiving under 200 r is less than that observed in the series reported by Simpson ($p < 0.05$), and may well not exceed that in the general population ($p < 0.01$).

Why should there be such a difference in cancer incidence in these two groups of children treated with comparable doses of x-rays? There are two plausible explanations. The first is that the children with

enlarged thymus were a selected group, whereas those in the present series were largely unselected. It is conceivable that there is a constitutional factor in the former group which predisposes to the development of cancer or leukemia. This could be confirmed or ruled out with certainty if the leukemia incidence were determined in children in whom thymic enlargement was diagnosed but untreated by radiation. Since a group of this nature of sufficient size for adequate study has not yet been located, the possibility of such an investigation is remote. However, a survey of children treated with x-rays in Rochester, N. Y., for various nonmalignant conditions has disclosed a high incidence of leukemia, including 2 cases in 75 children irradiated for pertussis (13). Since the dosage for pertussis was the same as for thymic enlargement, it seems likely that doses in this range may be leukemogenic, and that the condition for which the treatments were given was incidental.

The second explanation is dependent upon the port size used in the two series of cases. In the present series, the beam, measuring 4 × 4 cm., was much smaller than that generally employed in treating the thymus. In 2 of the 4 children in Simpson's series in whom leukemia developed after exposure to 200 r or less, the dose was 150 r and the port sizes were 6 × 8 and 6 × 9 cm. The third and fourth children received 100 and 200 r, respectively, through 10 × 10-cm. ports. Thus, in these children the mass of tissue irradiated was at least three times that in the children of the present series and included bone marrow in the sternum and anterior sections of the ribs. It seems possible, therefore, that the small treatment fields used in the present study could explain the apparent noncarcinogenicity of these exposures.

SUMMARY

A survey was made of 1,564 children in Pittsburgh given x-ray treatments to the thymus gland as a routine between 1938 and 1946. In 224 children, the diagnoses of enlarged thymus glands was made at birth. Eighty per cent of these were treated with 200 to 450 r of 140-kvp x-rays through a 4 × 4-cm. port. Ninety-five per cent of the 1,340 children with thymus glands of normal size were given 150 r through a port of the same size. Between 1956 and 1958, the families of 89.6 per cent of the treated children were questioned about the medical histories of these children and of their 2,923 untreated siblings. Positive medical data were confirmed but negative data were not tested. The death records of the Pennsylvania State Department of Health were also searched, as were the leukemia records from 1954 to 1957.

No cases of malignant disease were found in the treated group, although 4 cases of cancer, including 1 of leukemia, would be expected to occur in a group of children of this size and age distribution. The 4 malignant tumors in the sibling group, including 1 case of leukemia, compared closely with the expected number.

Because of the method of study and the absence of definitive information for 10 per cent of the treated children, the incidence of neoplasia in this group can be compared with that in the general population only with certain reservations. Nevertheless, it seems likely that the cancer and leukemia incidence in the treated children is not greatly increased over the expected incidence. The data obtained can be compared directly with that in untreated siblings and in irradiated children reported elsewhere for whom the same technic of study was employed. The cancer and leukemia rate is not significantly lower than that in the untreated siblings group, but is significantly below that in other children given comparable doses to the thymus gland through larger ports. It is suggested that the small port size (4× 4 cm.) used in treating these children could explain the difference in incidence of neoplasia in this group of children and that in those previously studied.

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SUMMARIO IN INTERLINGUA

Le Presente Stato de Salute de Juveniles Tractate in Lor Infantia con Radios X al Mediastino Anterior

Inter junio 1944 e maio 1946 micre doses de radiation X esseva administrate al region manubrial de neonatos, approximativemente 90 pro cento del serie total, al Hospital Pittsburgh, sin reguardo a si le thymo esseva allargate o de dimensiones normal. Le serie esseva revistate in 1956 a 1958, e al mesme tempore informationes esseva colligite con respecto al historia medical de non-irradiate fraternos del juveniles in question.

In 80 pro cento del 224 casos de allargamento thymic, le dose de radiation esseva 200 a 450 r (140 kvp) per un porta de 4 × 4 cm. In 95 pro cento del casos de normalitate dimensional del thymo, 150 r esseva applicate per un porta del mesme dimensiones.

Nulle caso de morbo maligne esseva trovate in le gruppo tractate, ben que le expectate incidentia, secundo le numero de casos e le distribution per etates, esserea 4 occurrentias de cancere, incluse 1 de leucemia. In le non-tractate fraternos, le observate incidentia de 4 casos de cancere, incluse 1 de leucemia, esseva nettemente de accordo con le numeros expectate.

Le reduction del incidentia de cancere e leucemia in le tractate gruppo in comparation con le gruppo del non-tractate fraternos non es statisticamente significative. Illo es significative, del altere latere, in comparation con altere reportate series de casos tractate con comparabile doses de radiation per plus grande portas. Es opinate que le micre porta usate in le presente serie, resultante in un reduction del volumine de tissu irradiate, explica possibilemente le plus basse incidentia de neoplasia.

Perivascular Extravasation of Thorotrast

Report of a Case With Eleven-Year Follow-Up[1]

LUTHER W. BRADY, M.D.,[2] DECK E. CHANDLER, M.D.,[3] ROBERT O. GORSON, M.S., and JOHN CULBERSON, M.D.[4]

VARIOUS complications have been reported following the diagnostic use of colloidal thorium dioxide (Thorotrast) since its introduction by Radt (9) in 1929. These have included aplastic anemia, thrombosis, and the production of sarcomata (3, 4, 5, 7, 8, 14). By far the most frequent complication, however, has been the formation of fibrous nodules and masses following inadvertent perivascular injection of the radioactive medium (1, 2, 6, 10, 11, 15, 16, 17).

This communication is concerned with a case in which sequelae of major import developed eleven years after the injection of Thorotrast into the soft tissues of the neck during attempted carotid arteriography. Of special interest is an estimate of the total tissue radiation dosage, made according to the method suggested by Rundo (13).

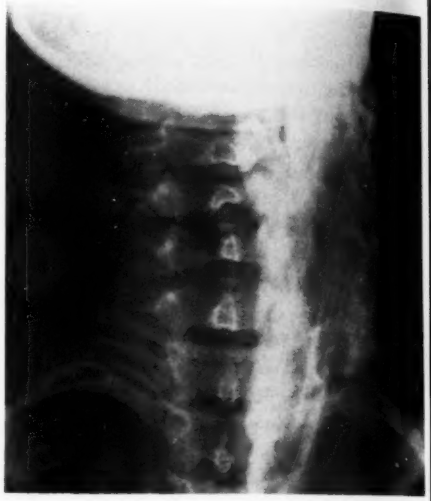

Fig. 1. Roentgenogram, June 14, 1945, showing extravasation of Thorotrast into the soft tissues of the left side of the neck. This occurred at the time of the unsuccessful attempt at left cerebral arteriography.

CASE REPORT

A 35-year-old white woman was first admitted to the hospital in June 1945, complaining of sudden onset of severe frontal headache during exertion. Shortly thereafter she experienced aphasia, incontinence, and a right hemiplegia. Three days after admission an attempt at cerebral arteriography with Thorotrast was unsuccessful. Six milliliters of the medium were extravasated into the soft tissues of the left side of the neck (Fig. 1). A subsequent arteriogram showed poor filling of the left anterior and middle cerebral arteries. This suggested an aneurysm near the junction of the anterior cerebral and carotid arteries. The patient improved rapidly and was discharged with the diagnosis of probable rupture of a congenital cerebral vascular aneurysm.

With the exception of a "lump in the left side of the neck," the patient was well until April 1955, when hoarseness developed within a few hours. This continued and became progressively more marked. In February 1956, difficulty in the use of the tongue was noticed. In October, the patient was readmitted for evaluation of her symptoms and of the left cervical mass.

Physical examination on admission revealed a Horner's syndrome on the left and atrophy of the left half of the tongue. A hard mass was palpable in the left side of the neck, extending from the posterior edge of the clavicle to the angle of the mandible. There were minimal right facial weakness and a right foot drop, but no sensory changes were noted. Laryngoscopy disclosed a left vocal cord paralysis.

Routine laboratory determinations were all within normal limits. Roentgenograms showed residual radiopaque material in the left side of the neck, extending into the superior mediastinum (Fig. 2). The spleen and liver were also shown to contain radiopaque material (Fig. 3).

Because of the possibility of continued expansion of the cervical lesion with ultimate involvement of vital structures, and in view of possible neoplastic transformation, surgical excision was performed in January 1957. A hard, calcified mass involving the

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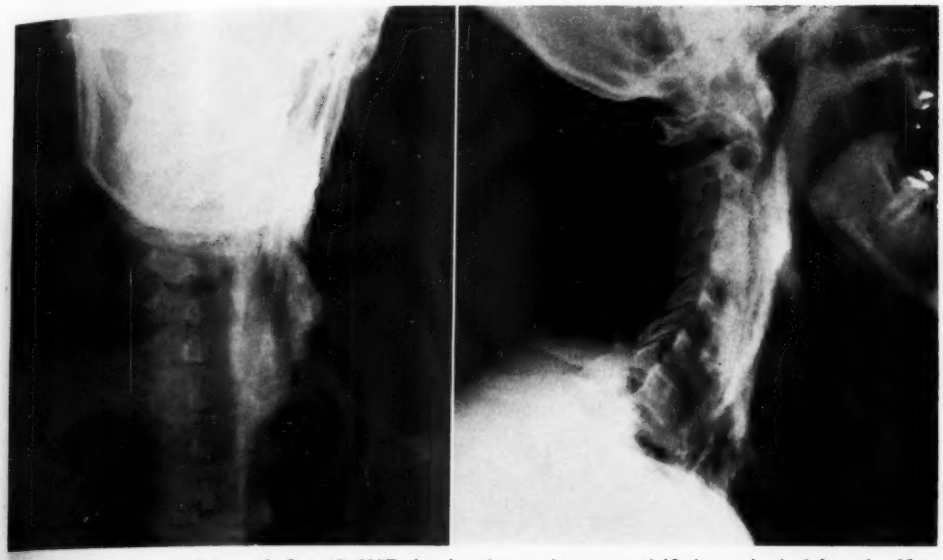

Fig. 2. Roentgenograms of the neck, Jan. 15, 1957, showing the conglomerate calcified mass in the left neck. Note that the shadow extends from the base of the skull into the left superior mediastinum.

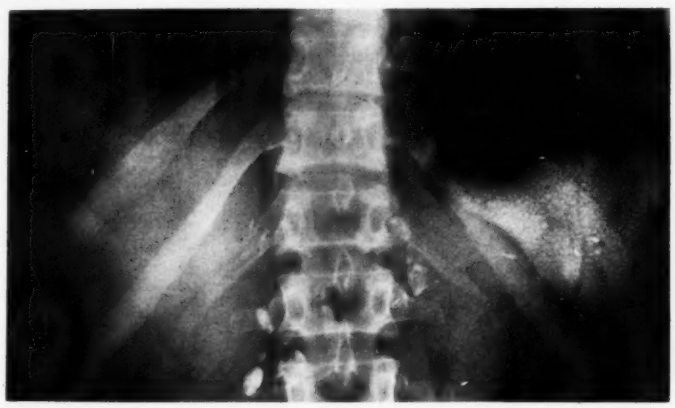

Fig. 3. Roentgenogram of upper abdomen, Oct. 23, 1956, showing deposits of Thorotrast in the liver and spleen.

carotid region was encountered, which extended superiorly to the foramen lacerum and inferiorly into the superior mediastinum. With sacrifice of segments of the carotid arteries, the jugular vein, and the vagus nerve, the mass was dissected free of the esophagus and trachea, to which it was firmly adherent. Its mediastinal portions were removed except for a portion about the subclavian artery. The hypoglossal nerve was sacrificed, but the phrenic nerve, which was uninvolved, was left intact.

The patient recovered rapidly following the surgical procedure, with no increase in neurological deficit. To date she has shown no evidence of recurrence of the mass or of progression of the findings (Fig. 4).

Pathologic examination of the operative specimen showed a very hard, amorphic, yellowish-white, rectangular mass weighing 46 gm., encased in the medial aspect of which were segments of the common and internal carotid arteries, the internal jugular vein, and the vagus nerve (Figs. 5 and 6). The hypoglossal nerve trunk entered the mass near its superior end. Extensive calcification of the specimen was noted with marked narrowing of the carotid and jugular vessels.

Microscopic sections showed relatively acellular and avascular, focally calcified collagenous and reticular connective tissue, throughout which innumerable gray-brown, refractile Thorotrast gran-

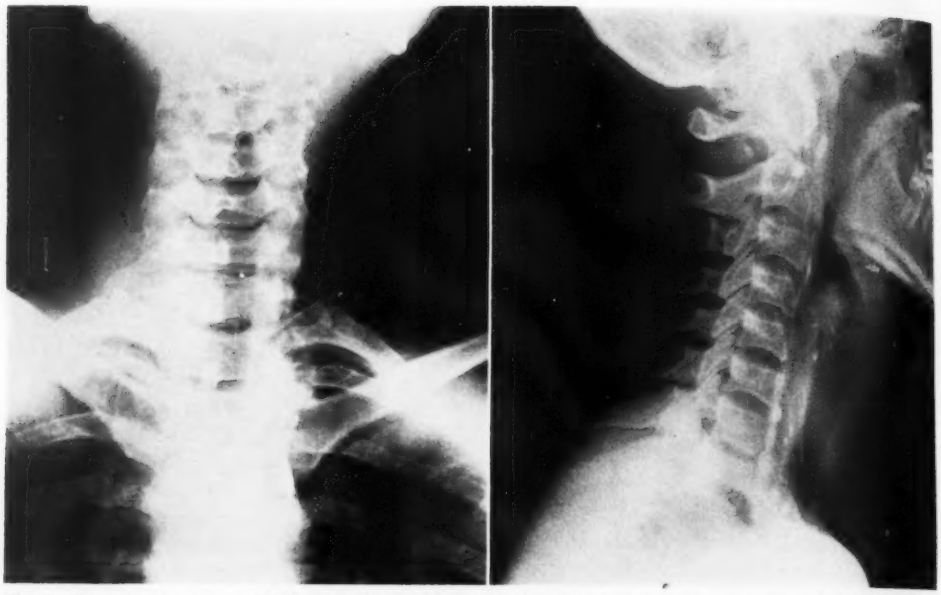

Fig. 4. Roentgenograms made following the surgical removal of the left neck mass, showing residual shadows in the left neck. The largest portion of the calcified conglomerate mass has been removed.

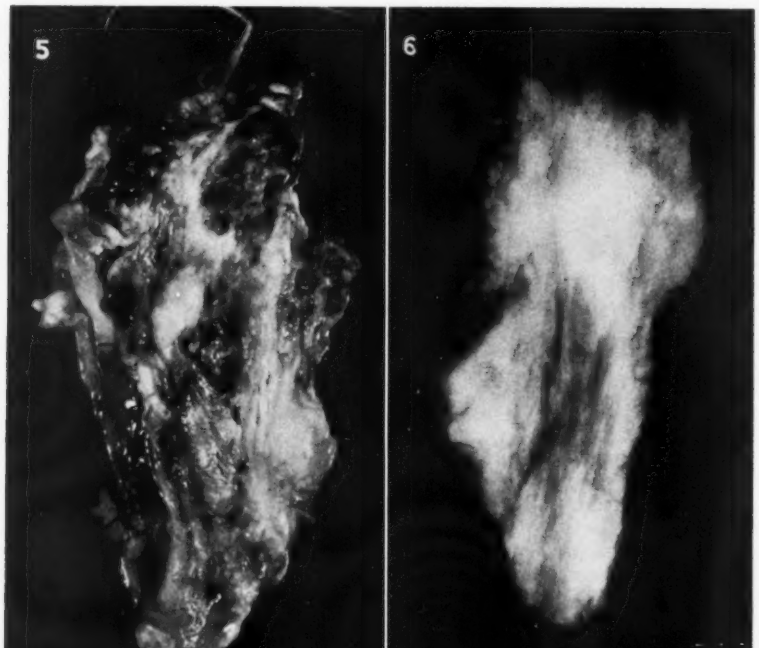

Fig. 5. Gross photograph of the excised specimen, demonstrating a portion of the left carotid artery. The hypoglossal nerve enters the mass superiorly.

Fig. 6. Roentgenogram of the surgical specimen, showing a lack of uniformity in the density of the mass.

ules of varying size were present (Fig. 7). These granules were both free in the tissue and within elongated histiocytes. There was no evidence of an active inflammatory process, continuing fibrous tissue proliferation, or of malignant transformation. Atypical post-irradiation fibrocytes were notably absent.

The carotid and jugular vessels were compressed by the adjacent fibrous tissue. Small arteries and veins likewise appeared to be compressed, and some of the arteries showed hyaline thickening.

Staining by the Weil technic (Fig. 8) revealed absence of myelin within the segments of cranial and sympathetic nerves present in the sections. Axis cylinders in the same nerves stained irregularly and poorly with the Bodian method.

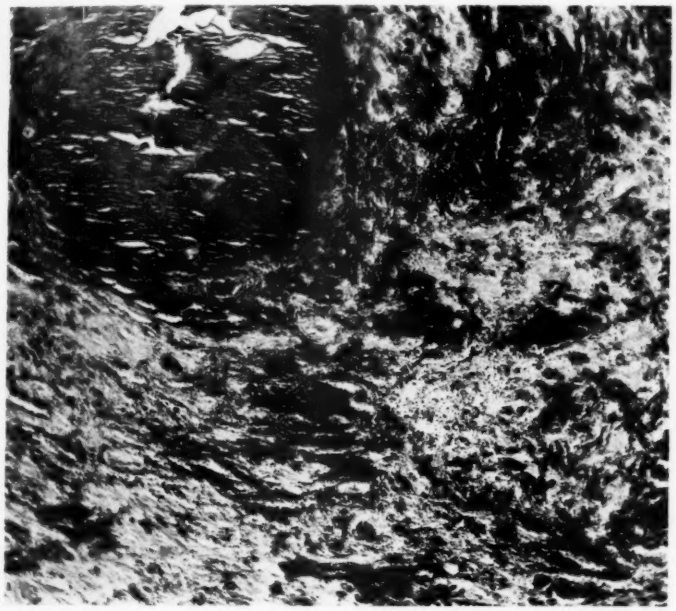

Fig. 7. Photomicrograph of a representative area in the excised lesion, showing Thorotrast granules within the amorphous scar. An area of calcification is noted at the upper left. Hematoxylin and eosin. (× *c.* 115)

CALCULATION OF ABSORBED DOSE

The thorium content of the excised tissue was estimated by radioassay comparison with a sample of aged thorium nitrate. Twenty-four grams of tissue were macerated and placed in test tubes for determination of the gamma and bremsstrahlung activity in a well-type scintillation counter. The standard for comparison was prepared by dissolving a weighed amount of thorium nitrate in water in another test tube. The relative activity of the tissue samples and standard was determined under the same counting conditions. The counting rates of the samples varied by a factor of three, indicating that the concentration of thorium probably varied widely throughout the specimen. The mean value for the radioassay was 0.018 gm. of thorium per gm. of wet tissue. The total amount of tissue involved in the extravasation was estimated to be 70 gm., of which only 46 gm. were excised. If it is assumed that the tissue not available for measurement had the same average thorium concentration, then the calculated total thorium extravasated was 1.26 gm., corresponding to approximately 6 ml. of Thorotrast. This value agrees favorably with the amount of Thorotrast estimated to have been extravasated at the time of the first cerebral arteriogram.

The activity of a thorium sample as determined by radioassay technics depends upon the degree of equilibrium that exists, at the time of assay, between the radio-

active daughter products and the parent isotope, thorium 232. The absorbed dose also depends upon the fractional distribution of the daughter isotopes during the exposure period. Rotblat and Ward (12) and Rundo (13) have shown that equilibrium conditions do not always exist in Thorotrast. Since the ratios of the radioactive decay products of thorium 232 are not known in the Thorotrast given the patient in 1945 nor in the tissue excised eleven years later, there is an uncertainty in the radioassay and in the calculated absorbed dose. The absence of equilibrium conditions in the tissue would lead to an underestimation of the thorium content. The absorbed dose, however, would be overestimated, so that the errors would tend to compensate. For calculation purposes, therefore, it was assumed that isotopic equilibrium did exist in both the Thorotrast given to the patient and in the tissue at the time of operation.

The absorbed dose estimates were made from Rundo's graphs (13), which show the accumulated alpha and beta energy emissions from thorium preparations as a function of time. The total dose from 0.018 gm. of thorium 232 and 228 per gm. of tissue over eleven and a half years is 9,200 rads from alpha radiation and 250 rads from beta radiation. (If thorium 228 was not present initially, then the corresponding absorbed doses would have been approximately 5,800 rads from alpha radiation and 200 rads from beta radiation.) The dose from gamma radiation is comparatively insignificant.

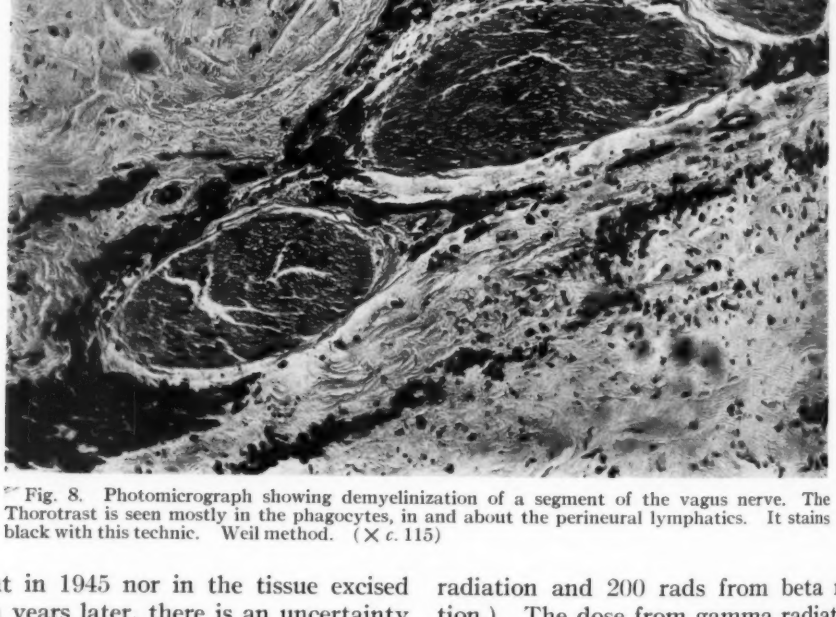

Fig. 8. Photomicrograph showing demyelinization of a segment of the vagus nerve. The Thorotrast is seen mostly in the phagocytes, in and about the perineural lymphatics. It stains black with this technic. Weil method. (× *c.* 115)

The calculated dose values require a correction for self-absorption of the alpha particles in the thorium dioxide granules. This effect may reduce the tissue dose from alpha radiation by 50 per cent or more (12, 13). Taking the various approximations and assumptions into account, the best estimate of the average absorbed dose appears to be 4,000 to 5,000 rads.

COMMENT

This case, like several of those reported

by Amory and Bunch (1), illustrates the serious potential danger of extravasation of Thorotrast into tissues containing important structures. After an asymptomatic period of ten years, involvement of the vagus, hypoglossal, and cervical sympathetic nerves became clinically evident, apparently as a result of demyelinization and degeneration consequent to pressure from the fibrous mass in which they lay. In addition, stenosis of the carotid and jugular vessels was present on pathologic examination.

The changes noted following Thorotrast injection into soft tissue are similar to those described by others (1, 2, 6, 10, 11, 16, 17). Following initial infiltration of the area by polymorphonuclear leukocytes (11), phagocytosis by histiocytes takes place and is followed rather rapidly by production of fibrous tissue. The extent of the involved area may increase subsequently, apparently as Thorotrast-bearing macrophages carry pigment away from the injection site. Necrosis often occurs, probably because of the presence of foreign material, and the foci of calcification frequently noted radiologically and pathologically are probably within such areas. With aging of the connective tissue, the consequent mass becomes hyalinized and denser. The whole process seems quite analogous to the foreign-body type reaction caused by certain other materials, such as silica.

It is noteworthy that, in spite of the tissue dosage of 4,000 to 5,000 rads estimated to have been delivered over a period of eleven and a half years, there was no definite pathologic evidence of radiation effect. Rather, the picture remains one identical with the foreign-body type reaction noted in cases of lesser duration.

SUMMARY

1. A case is presented in which Thorotrast extravasation during attempted carotid arteriography was followed ten years later by loss of function of cranial and cervical sympathetic nerves.

2. An estimate of absorbed radiation dosage was made from the surgically excised tissues.

3. Pathologic findings are described and are interpreted as representing a foreign-body reaction. No evidence of radiation effect was noted.

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(*Pro le summario in interlingua, vider le pagina sequente*)

SUMMARIO IN INTERLINGUA

Extravasation Perivascular de Thorotrast: Reporto de un Caso con Dece-Un Annos de Observation Sequential

Es reportate un caso in que extravasation de Thorotrast occurrente durante un tentativa de arteriographia carotidic esseva sequite dece annos plus tarde per un perdita de function de nervos sympathic cranial e cervical. Un massa calcificate dur, que se extendeva in alto usque al foramine lacere e in basso usque a in le mediastino superior, esseva incontrate al operation. Illo esseva excidite partialmente. Incastrate in le massa esseva segmentos del arterias carotidic commun e interne, del interne vena jugular, e del nervo vage. Le trunco del nervo hypoglossal entrava in le massa in le vicinitate de su termination superior.

Le quantitate total del thorium extravasate es calculate a 1,26 g, e le absorbite dose de radiation es estimate a inter 4.000 e 5.000 rad in le curso del dece-un annos precedente le ablation del massa.

Le constatationes pathologic es interpretate como representante un reaction a corpore extranee. Nulle prova de effectos de radiation esseva observate.

Spent Radon Seeds: I. Late Effects[1]

JOHN B. GRAHAM, M.D., RUTH M. GRAHAM, Sc.D., LUCIANO S. J. SOTTO, M.D., and NORMAN A. BAILY, Ph.D.

SPENT RADON seeds are generally regarded as being inert. Actually, they continue to emit measurable radiation for many years. We have had several patients recently with a late complication or recurrence following treatment of cancer of the cervix with radon seeds. The possibility of a connection between the residual radiation and the complications cannot be ignored.

The unique properties of radon were recognized and led to the use of this agent almost from the beginning of radiotherapy. Its popularity was understandable, for it gives the same radiations as radium but decays with a half-life of 3.8 days and so may be permanently implanted. It seemed ideal for a number of situations. Radon seeds have been implanted in and about untold thousands of cancers. The results have been satisfactory and there has been no reason to believe that patients treated in this way are any more prone to late complications than those given other forms of radiotherapy. It is well known that radon degenerates into radium C, D, and E, that radium D has a half-life of nineteen years, and that all of these forms are radioactive. However, this residual activity was dismissed as of no consequence because it is mainly alpha or beta and so usually does not escape through the gold sheath.

In a recent three-month period we have encountered one vesicocervical fistula, apparently due to radiation, nineteen years after insertion of radon seeds for cancer of the cervix, and 3 recurrences of tumor twelve, twenty, and twenty-one years after the implantation of radon seeds in the cervix. The occurrence of these complications so long after radiotherapy is unusual. All of the patients had detectable radiation from the retained seeds.

CASE REPORTS

CASE I (Hog): A 38-year-old colored woman was first seen in December 1939 with a squamous cancer of the cervix, Stage IV, with bladder involvement. On Dec. 29, she was treated with radium in the uterine and cervical canal, 2,400 mg. hr. (200 mg. radium, 4 cm. active length, 1 mm. Pt filtration, twelve hours), and 9 gold radon seeds: 6 with a strength of 1.5 mc and 3 of 1.6 mc, giving a total of 13.8 mc. She was well and symptom-free for sixteen years, at the end of which time symptoms of bladder irritation occurred. These gradually progressed, and in June 1958 a vesicocervical fistula developed, eighteen and a half years following treatment.

Study of the patient showed a nonfunctioning left kidney and hydronephrosis of the right. The vaginal smear showed precornified cells with malignant nuclei and 7 per cent radiation-response cells. Biopsies were negative for tumor. Six seeds were visible on the x-ray film and, when scanned[2] for radioactivity, the pelvis gave a count 25 per cent above the background. On Aug. 29, 1958, an anterior exenteration was performed and the urinary stream diverted through an ileal loop to the sigmoid. No tumor was found in the specimen. The seeds were recovered.

CASE II (Rob): A 43-year-old woman had a Stage-II squamous cancer of the cervix treated on Sept. 16, 1933, with radium in the cervical canal, 2,400 mg. hr. (200 mg. radium, 4 cm. active length, 1 mm. Pt, twelve hours) and radon gold seeds: 4 of 1.0 mc, 1 of 1.1 mc, 4 of 1.2 mc, 3 of 1.25 mc, giving a total of 13.65 mc. On Jan. 5, 1934, a small residual nodule anterior to the cervix was treated with a single gold seed of 1.0 mc. A recurrence of squamous carcinoma in December 1954 was treated by x-rays, 5,600 r depth dose in five weeks, and was controlled for a time. It recurred massively in 1958 and the patient died on Oct. 5, 1958. In September 1958 she had a positive vaginal smear that showed 31 per cent radiation response. When scanned, her pelvis was found to have an emission 85 per cent above the background level. The seeds were recovered postmortem.

CASE III (Car): A 52-year-old woman had a squamous cancer of the cervix, Stage II. She was treated with 1,000-kv x-rays, full pelvis, receiving 4,800 r in the region of the cervix from Sept. 3 to Oct. 15, 1946, and 10 radon seeds of 1.2 mc

[1] From Roswell Park Memorial Institute, Buffalo, N. Y. Accepted for publication in April 1959.
[2] With a 1.5 × 1.5 inch sodium iodide crystal scintillation counter.

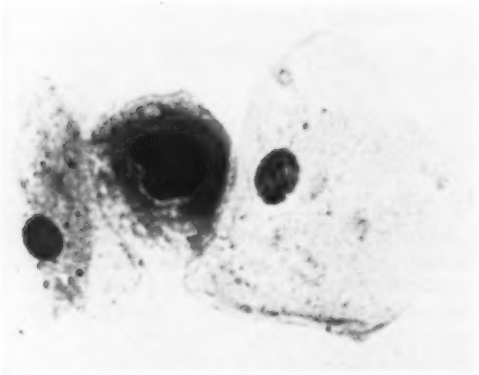

Fig. 1. Exfoliated cells from a vaginal smear. The cell in the center shows abnormal chromatin distribution plus an increase in chromatin. Compare with benign nucleus to the right. (×275)

each on Sept. 13, 1946. She was well until 1958, when she was seen with a recurrent pelvic tumor, for which she was given palliative radium in the uterine canal and vagina, 3,000 mg. hr., on May 21, 1958. She died on Oct. 23, 1958, with massive pelvic and abdominal tumor. The seeds were recovered. Two weeks prior to death the vaginal smear showed a radiation response of 21 per cent and the pelvis exhibited radiation 24 per cent above background.

CASE IV (Bro): A 38-year-old woman had a Stage-III squamous carcinoma of the cervix treated on March 19, 1947, with 10 radon seeds of 1 mc each, from March 25 to April 30, 1947, with x-rays, 4,680 r depth dose, and on April 30, 1947, with 3,950 mg. hr. of radium in the cervical canal 50 mg., 79 hr., 1 mm. Pt. She remained well, with no symptoms. In June 1958 her vaginal smear was positive for squamous carcinoma and showed 4 per cent radiation response. Her pelvis exhibited radiation 137 per cent above background. On Oct. 5, 1958, a hysterectomy was performed and the seeds were recovered.

CASE V (Jen): A 56-year-old woman had a Stage-II cancer of the cervix treated in May 1938 with x-rays, 2,195 r depth dose. On June 2, 1938, 9 radon seeds (1 of 1.1 mc, 8 of 1.2 mc) were inserted, and radium, 2,400 mg. hrs. (200 mg. 4 cm. active length, 1 mm. Pt, 12 hours) was given in the cervical canal. A recurrence with vesicovaginal fistula developed in 1958. At that time the pelvic radiation was 48 per cent above background. The tumor was too far advanced for further treatment.

DISCUSSION

Recurrences after radiotherapy for cancer of the cervix develop most frequently in the first year, with a steady decline in incidence thereafter. For example, in a series of 2,436 patients treated at the Radium Center in Copenhagen during the years 1922 to 1937, Truelsen found only 38 recurrences appearing after five years. Of these, 32 developed between the sixth and tenth years, 5 in the eleventh to fifteenth year, and 1 in the sixteenth year following treatment. Recurrence after fifteen years is distinctly rare. The longest interval is reported by Howkins and Andrew, whose patient had a recurrence thirty years after radium therapy.

Late radiation complications are equally uncommon. Less than 10 per cent occur more than five years after radiotherapy for cancer of the cervix. In Truelsen's series, the latest vesicovaginal fistula was seen at twelve years. Corscaden had a patient in whom a fistula developed twenty-two years after radium was applied.

Our attention was first attracted by a patient who was seen with a vesicocervical fistula and progressive ureteral obstruction, apparently due to radiation, nineteen years after treatment. This was a bizarre situation, and in an attempt to explain it, we suspected the radon seeds of some residual activity, which was confirmed when the patient was tested.

The three patients in whom recurrent tumor developed twelve, twenty, and twenty-one years respectively after treatment were also somewhat unusual. One patient with late recurrence would be unremarkable, but 3, all in patients with measurable ionizing radiation in the pelvis, suggested a possible relation between continued irradiation and the development of recurrence or fistula. We had naively assumed that spent radon seeds would be entirely inert and we were somewhat astonished to find them active enough to be measured by simple scanning technics.

The nuclear medicine department at Roswell Park Memorial Institute was kind enough to scan 18 patients with seeds implanted between 1930 and 1947, with a scintillation counter such as is used to measure I^{131} uptake in the thyroid. Three

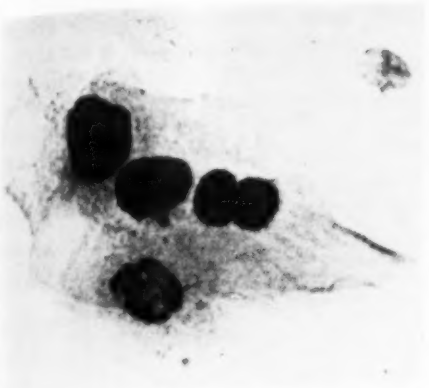

Fig. 2. This large cell has four abnormal nuclei of different size plus a single degenerating nucleus. (X275)

showed no activity, the remaining 15 exhibited pelvic radiation ranging from 16 to 137 per cent above background.

Radon seeds are apparently tolerated by the tissues for long periods of time, for the only report to the contrary we have encountered is that of Downing and Folan, who recorded a case of ulceration and discharge of seeds twenty years after implantation in the chin. No mention was made of residual activity. Fourteen out of 18 patients showed loss of seeds as evidenced by a smaller number visible in the x-ray films than were originally inserted. The number lost varied from one to six.

H. E. Johns and L. D. Skarsgard of the University of Toronto and R. E. Evans, H. W. Kraner, and J. L. Bear of the Massachusetts Institute of Technology examined the seeds and determined the spectrum of radiation (see following paper by Johns and Skarsgard). They showed that the beta rays of 1.17 Mev emitted by radium E strike the gold and generate a continuous spectrum of x-radiation with peaks at 70 kev and at 167 kev. These x-rays are of a very low intensity, delivering only 100–300 rads in the years after their initial activity subsided. Two factors operate to cloud our evaluation of this dose in terms of conventional exposures. One is that the tissues were heavily irradiated initially and so may not respond as normal tissue would to this amount of radiation. The

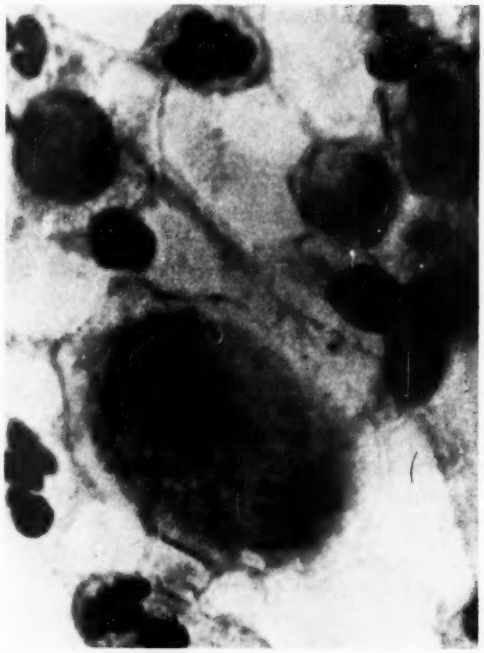

Fig. 3. Mitotic figure seen in the vaginal smear of a patient in whom radon seeds had been implanted many years previously. (×725)

second is that the radiation has been maintained over many years at a fairly constant rate and may exert quite a different effect than radiation given in a shorter period.

Evidence of the biological effect of this apparently trivial amount of radiation is circumstantial. In 5 patients out of a total of about 250 seed cases being followed in our clinic, unusual complications arose. However, the exfoliated cells of the vaginal smears in patients with seeds present a unique appearance (Figs. 1–3). The squamous epithelial cells were increased in size; the nuclei were abnormal, with irregular chromatin, as in a malignant process; there were multiple nuclei, and mitoses were present. This is a picture reminiscent of carcinoma *in situ*. The smears of 22 cervical cancer patients in whom radon seeds had been implanted more than fifteen years earlier were examined. For comparison, smears were taken from patients who had been treated with radium and x-rays during the same period. Multiple

nuclei were encountered in 12 radon cases and in only 4 radium cases. Keratin, as evidenced by an orange-staining cytoplasm (with Papanicolaou's stain) was found in 9 radon and 2 radium cases. In nonirradiated patients, keratin is found only in the presence of cancer. Karyorrhexis, a degenerative change, was found in 9 radon and 4 radium patients. Mitoses, rarely seen in vaginal smears, were encountered in 3 radon patients. None were found in the radium cases. This cytologic picture tends to support the view that spent radon seeds have some biologic activity, either destructive or carcinogenic.

The history of medical usage of ionizing radiation is replete with practices that were at first regarded as innocuous but subsequently proved hazardous. It is possible that spent radon seeds may be another example of a practice that is not entirely free from danger. Certainly they would bear more thorough investigation.

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SUMMARIO IN INTERLINGUA

Capsulas de Radon Extincte. I. Effectos Tardive

Es reportate cinque casos in que un tardive complication o recurrentia sequeva per multe annos le implantation de capsulas a radon in le tractamento de carcinoma del cervice uterin. Le possibilitate non pote esser rejicite que il existe in iste casos un connexion inter le radiation residue ab le implantate capsulas e le complication o recurrentia del tumor. Le scrutinio radiometric del pelve in le hic-reportate casos monstrava un activitate radiatori de inter 24 e 137 pro cento supra le nivello de fundo. Frottis vaginal exhibiva un imagine de character unic. Le squamose cellulas epithelial esseva grande. Le nucleos esseva anormal con irregularitate del chromatina, como in un processo maligne. Nucleos multiple e mitoses esseva presente. Iste tableau suggere carcinoma in sito.

Le calculation del radiation ab le extincte capsulas obtenite in iste casos es le thema del sequente articulo.

Spent Radon Seeds: II. Radiation from Spent Radon Seeds[1]

H. E. JOHNS, Ph.D., and L. D. SKARSGARD, M.Sc.

RADON decays with a half-life of 3.82 days. Thus, in a period of two months, it should decay by a factor of about 6.4×10^4 and so have negligible activity. The decay process involves the following transformations:

$$\underset{}{\text{Rn}} \xrightarrow[3.82\ \text{days}]{} \text{Ra A} \xrightarrow[3.05\ \text{min.}]{} \text{Ra B} \xrightarrow[26.8\ \text{min.}]{} \text{Ra C} \xrightarrow[19.7\ \text{min.}]{} \text{Ra C}^1$$

$$\text{Ra C}^1 \xrightarrow[10^{-4}\ \text{sec.}]{} \text{Ra D} \xrightarrow[19.4\ \text{yr.}]{} \text{Ra E} \xrightarrow[5.00\ \text{days}]{} \text{Ra F} \xrightarrow[138\ \text{days}]{} \text{Pb}$$

Since all the transformations from radon to Ra D are of short half-life, after about two months all the activity will be in the form of Ra D. If we start originally with 1 mc of radon, giving 3.7×10^7 dis/sec., then after about two months we will have Ra D with initial activity as follows:

Activity of Ra D per initial mc radon =

$$3.7 \times 10^7 \frac{3.82}{19.4 \times 365} = 1.99 \times 10^4 \text{ dis/sec} \quad (1)$$

Ra D and its daughter products will then decay, with the half-life of Ra D (19.4 years). Ra D decays, with the ejection of a soft beta particle (17 kev), into Ra E, which in turn decays, with the emission of a beta particle with maximum energy 1.17 Mev, into Ra F. Ra F then decays with the ejection of an alpha particle of energy 5.3 Mev. Since none of these transformations involve gamma rays, we would not, on cursory glance, expect any activity from a spent radon seed.

However, in the slowing down of the beta particle in the gold sheath, bremsstrahlung is produced. Wyard (5) has shown that the energy E_γ radiated in Mev per beta particle is given by:

$$E_\gamma = 1.23 \times 10^{-4} (Z + 3) E_\beta^2 \quad (2)$$

where E_β is the maximum energy of the beta particle in Mev and Z the atomic number of the material in which the particle is stopped.

Combining Equations 1 and 2 and substituting values, we find that the energy radiated per initial mc of radon is:

$$E_\gamma = 2.74 \times 10^2 \text{ Mev/sec.} \quad (3)$$

The spectral distribution of this radiation, as given by Wyard, indicates that the spectrum extends from about 50 kev to 500 kev. Over this range the energy flux per roentgen is about 3,000 ergs/cm.^{2}/r. We thus obtain:

Exposure dose 1 cm. from 1-mc source =
1.16×10^{-8} r/sec. =
41.7 μr/hr. =
0.37 r/year (4)

Now 1 mc of radon gives an exposure dose of 8.25 r/hr. at 1 cm. Thus, the activity of the spent radon will be down by a factor of about 2×10^5 from its initial value. Although the activity is down by a factor of about 10^5, the half-life of Ra D is greater than that of radon by a factor of 1,850. Thus, the integrated dose from the spent radon may be expected to be less than that of radon by a factor of about 100.

The above calculations do not take into account the effects of filtration and must be considered only as a rough guide to the exposure dose expected from a spent radon seed.

MEASUREMENTS

Five spent radon seeds, each with an initial activity of 1.13 mc on Sept. 16, 1933, were taken from a patient (see Case II, Rob, in the preceding paper) and measured in December 1958. The meas-

[1] From the Departments of Physics and Medical Biophysics, University of Toronto, Toronto, Ont., Canada. Accepted for publication in April 1959.

TABLE I: SPECTRAL DISTRIBUTION OF THE RADIATION FROM SPENT RADON SEEDS AND CALCULATION OF EXPOSURE DOSE RATE

(5 seeds taken from a patient twenty-five years after implantation. Initial activity 1.13 mc.)

Channel Number	Mean Energy (Mev)	Photons/hr. per Steradian	Energy-flux (ergs/steradian per hour)	Energy Flux (ergs/cm.²/r	Dose Rate (μr/hr.)
2–9	0.059	3.93×10^5	0.0371	2,920	12.7
10–19	0.102	6.94	0.1134	3,600	31.5
20–29	0.209	4.51	0.151	3,090	48.9
30–39	0.300	2.19	0.105	2,910	36.2
40–49	0.390	1.01	0.0630	2,850	22.1
50–59	0.481	0.566	0.0436	2,830	15.4
60–69	0.572	0.244	0.0224	2,830	7.9
70–79	0.663	0.128	0.0136	2,850	4.8
Integrated dose rate					179.5

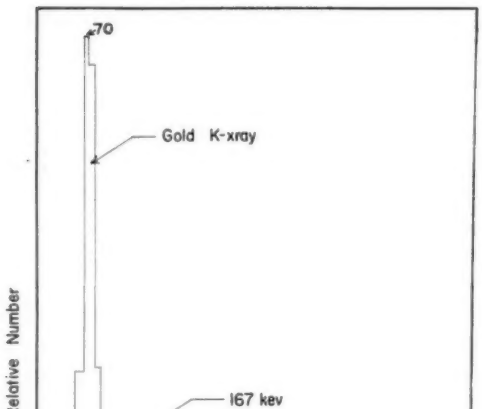

Figure 1

urements were undertaken with the seeds 8.2 cm. from a 2 1/2 × 3-inch sodium iodide crystal so arranged that the solid angle, subtended by the source, was 0.0187 steradians. Measurements were made on a 100-channel pulse-height analyzer and are shown in Table I and Figure 1. In Table I, the number of photons per hour per steradian is given for various energy intervals as shown in the third column. On the basis of the known energy flux per roentgen, the exposure doses in microroentgens per hour were calculated and are given in the last column of the Table. The total of this last column is 179.5 μr/hr. When this is corrected for the decay of the radium D for a twenty-five-year period, we obtain 435 μr/hr. at 1 cm. per 5.65 mc or 76.5 μr/hr. at 1 cm. per initial mc. This is not inconsistent with the approximate value predicted in Equation 4.

The spectral distribution shown in Figure 1 warrants some discussion. The intensity of the bremsstrahlung spectrum without filtration is maximum at zero energy and falls continuously as the photon energy is increased to reach zero at 1.17 Mev, the maximum energy of the beta particle. For similar spectra, see Evans (2), Lidén, Starfelt and Cederlund (1, 3, 4), and Wyard (5). However, when this continuous spectrum is filtered by gold, the low-energy end is drastically reduced because of the high absorption coefficient at low energies. In the region just above the K edge of gold (80.7 kev) the photoelectric coefficient in the K shell is large and the radiation in this part of the spectrum is therefore small. However, each photoelectric absorption gives rise to a hole in the K shell of an atom with the subsequent emission of K radiation with energies just below 80.7 kev.

This accounts in part for the peak at 70 kev. In addition, the beta particles themselves eject K electrons and so give rise to K radiation. Finally, in the region just below 80.7 kev, there is a "window" in the absorption coefficient so that more radiation from the continuous spectrum is trans-

TABLE II: EXPOSURE DOSE RATE OF SPENT RADON SEEDS PER INITIAL MC AT 1 CM. IN μr PER HOUR

Patient	Initial Activity (mc)	No. Seeds	Age of Seeds (years)	Decay Factor	Exposure Dose Rate at 1 cm. per Initial mc. μr/hr. At Present	At Time of Implant
Car	12.0	10	12	0.65	13.2	20.3
Rob	13.65	12	25	0.415	31.8	76.5
Bro	10.0	10	11.5	0.660	28.2	42.8
Hog	13.8	9	19	0.504	20.0	39.6

TABLE III: MEAN AND MAXIMUM ABSORBED DOSES

Patient	Volume Implant (c.c.)	Length Seed (mm.)	Age (years)	Absorbed Dose During Period Max rads	Mean rads
Car	1.2	2.5	12	89	66
Rob	11.0	5.0	25	326	148
Bro	1.6	3.5	11.5	152	93
Hog	5.0	4.5	19	167	80

mitted in this region. The large peak at 70 kev results from a combination of these three effects.

Spent seeds from 4 patients were measured by the method described above, and the results are shown in Table II. In the last column the activities of the seeds have been corrected for decay (half-life of 19.4 years), and the values represent the exposure dose rate in μr/hr. at 1 cm. a few months after the time of implant, when the initial radon activity will have decayed. The dose rates are not constant and vary by a factor of over three. The higher activities were found in the seeds with the larger physical dimensions. This is what one might expect, since the longer seeds contained more radon initially but were allowed to decay for a few days (half-life 3.83 days) until they reached the correct activity for an implant. This means that the bremsstrahlung activity can be predicted only if the initial activity of the radon a few hours after loading is known rather than the activity at the time of implantation.

From the data given in Table III, it is possible to estimate the maximum and mean absorbed doses in the region of the tumor due to the spent radon seeds. The maximum dose has been considered to be at a point 1 mm. from a single seed. The mean dose for the implant was calculated, on the assumption that the original implant followed a Paterson and Parker volume distribution. The calculations in the latter case can be considered to give only the order of magnitude, since the size of the implant will not have remained anything like constant over the period of time and, in addition, some of the seeds have been sloughed out.

Examination of the table will indicate that the doses range from about 100 to 300 rads over the ten- to twenty-year period. This dose is small and probably does not have too much significance. Yet, the possibility of it causing chronic irritation cannot be completely ruled out.

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SUMMARIO IN INTERLINGUA

Capsulas de Radon Extincte. II. Radiation ab Extincte Capsulas de Radon

Le dose de radiation que debe esser expectate ab extincte capsulas de radon es calculate super le base del processo disintegratori, e ver mesurationes del radiation ab capsulas recovrate ab certes del casos describite in le articulo precedente es reportate. In 4 casos, le doses esseva inter circa 100 e 300 rad in le curso del periodo de dece a vinti annos durante le qual le capsulas remaneva in sito. Durante que iste dose es probabilemente sin grande importantia, le possibilitate que illo resulta in un irritation chronic non debe esser negligite.

Multisection Transverse Tomography in Radium Implant Calculations[1]

ROBERT EGAN, M.D., and GORDON C. JOHNSON, M.D.[2]

THE PLANNING OF interstitial radium needle implants is usually based upon standard geometric forms. Anatomical limitations, tumor extension requiring supplemental needles, and technical imperfections result in implants somewhat at variance with standard geometry. Accurate delivery of planned dosage requires calculation from the completed implant rather than from the initial plan.

With standard radium distributions, or limited deviations therefrom, measurements from radiographs taken in perpendicular planes with the use of the Pythagorean theorem (1) are generally adequate for calculation purposes. For more marked deviations and for multiple or curved planes, the perpendicular projection technic (2) allows an accurate and more complete survey of needle distribution. This method requires identification of all needles on the radiographs. In multiple plane and large volume implants, identification of needles is difficult and in some cases impossible. In these cases, reconstructions from stereoradiographs (3) usually can be made, but at the expense of considerable time.

A "Siemens' Transversal Planigraph" (Fig. 1) was available in our department. It was conceived that the rotational feature would lend itself to the study of linear opaque objects such as radium needles which would not be as well demonstrated by conventional tomography using linear tube travel (Fig. 6). The areas of major clinical concern were the tongue, floor of the mouth, buccal mucosa, and neck. In these areas dosage levels were critical, accurate identification of large numbers of needles was difficult, and the axis of implants frequently paralleled the axis of the body. These factors suggested a trial of transverse tomography.

The basic equipment and technic of axial transverse tomography has recently been reviewed by Wilk (4). In our department, effort had been directed toward improvement in diagnostic detail. We had been unable to achieve film detail comparable to that of conventional tomography, but gross anatomy was well demonstrated. Various modifications (Fig. 2) facilitated clinical application and improved results. The tube stand-patient distance was increased and fixed to provide a constant low magnification factor and allow better beam alignment by eliminating one axis of motion, the horizontal tube travel. Limitation in a second axis of motion, vertical tube travel, also improved beam alignment. Variation for special clinical situations could be obtained by altering the angle of declination of the beam and by raising or lowering the patient in the rotating chair. Air compression bags originally furnished with the equipment allowed some shift of the patient during rotation. These were replaced by foam rubber pads, which reduced motion while providing adequate comfort. Motion of the head was minimized by addition of a radiolucent plastic extension head rest to which the head could be fixed. Radiographic shadows were reduced by elimination of the dense arm rests.

Initially, serial exposures were made by aligning the beam and cassette before each exposure. Change in position of the patient between exposures, however, invalidated direct comparison of the serial sections. Subsequently, a multiple cassette box was devised, using single intensifying

[1] From the University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas. Presented at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15-20, 1959.

[2] American Cancer Society Advanced Clinical Fellow in Radiotherapy.

Fig. 1. "Siemens' Transversal Planigraph" with patient in examining position. Tube stand-patient distance reduced for illustration.

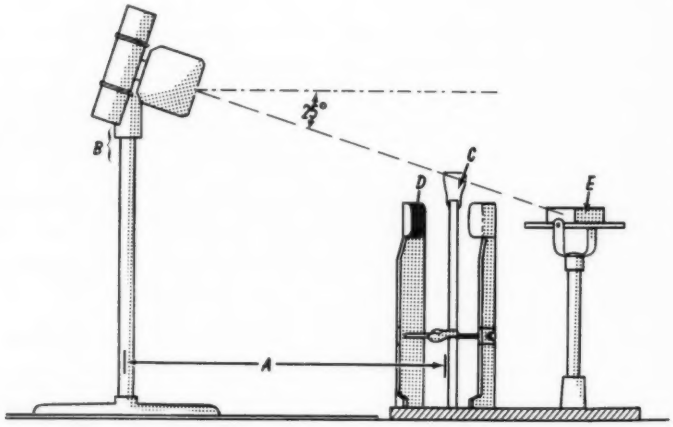


Fig. 2. Modifications of "Siemens' Transversal Tomograph" for multisection head and neck use. A. Tube stand-patient distance increased and fixed. B. Vertical tube travel limited. C. Radiolucent plastic head rest. D. Foam rubber pads. E. Multiple cassette box.

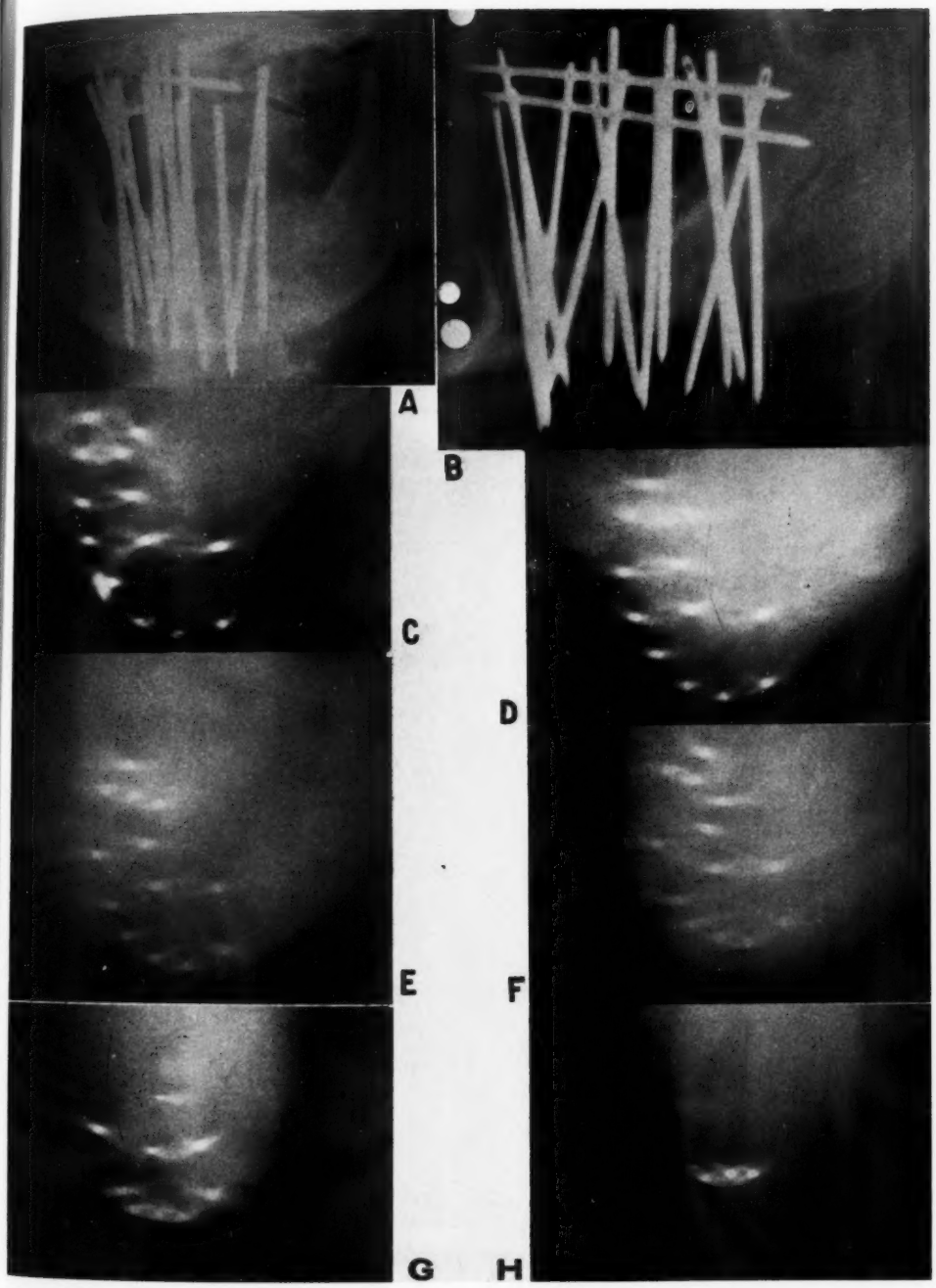
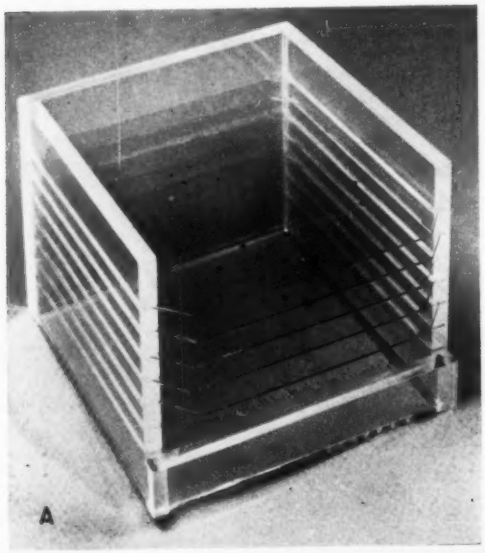


Fig. 3. Double plane implant in tongue. A and B. Routine radiographs. C-H. Serial transverse tomographic sections.

screens and low density spacers. After multiple cassette "books" with paired intensifying screens became commercially available, one of these containing seven layers was obtained and mounted in a balsa wood box. Films were spaced 1 cm. apart providing coverage of just over 5 cm. at the level of the implant. Film detail on individual cuts was lessened by the use of the multiple cassette, but sufficient detail remained to identify bony landmarks and to demonstrate clearly the positions of the radium needles. Obtaining multiple sections simultaneously relieved the need for precise alignment at the tumor level, and the serial sections matched perfectly (Fig. 3). A simple reconstruction technic was devised (Fig. 4) which facilitated a more complete analysis of the implants and proved to be a very useful teaching tool.

The method is now in regular clinical use (Figs. 5 and 7). Routine radiographic views are first obtained. When additional information is necessary or desirable, a single multisection tomographic exposure usually suffices. Comparison with the



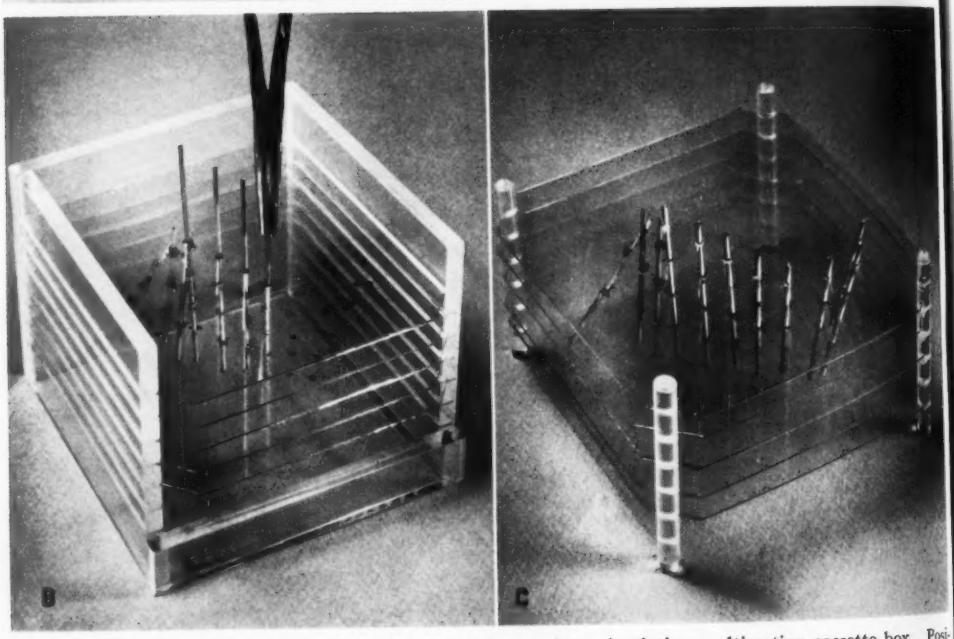


Fig. 4. Reconstruction technic. A. Slotted plastic template, simulating multisection cassette box. Positions of radium needles are traced as black dots on the plastic sheets, which are then positioned similar to the original radiographic films. B. Brass wires, simulating radium needles, are heated and plunged through the plastic sheets at points indicated by aligned black dots. C. The plastic sheets are fixed by the wires. The entire model may then be removed from the template. Corner posts are convenient for handling and filing. Magnification is uniform in all dimensions.

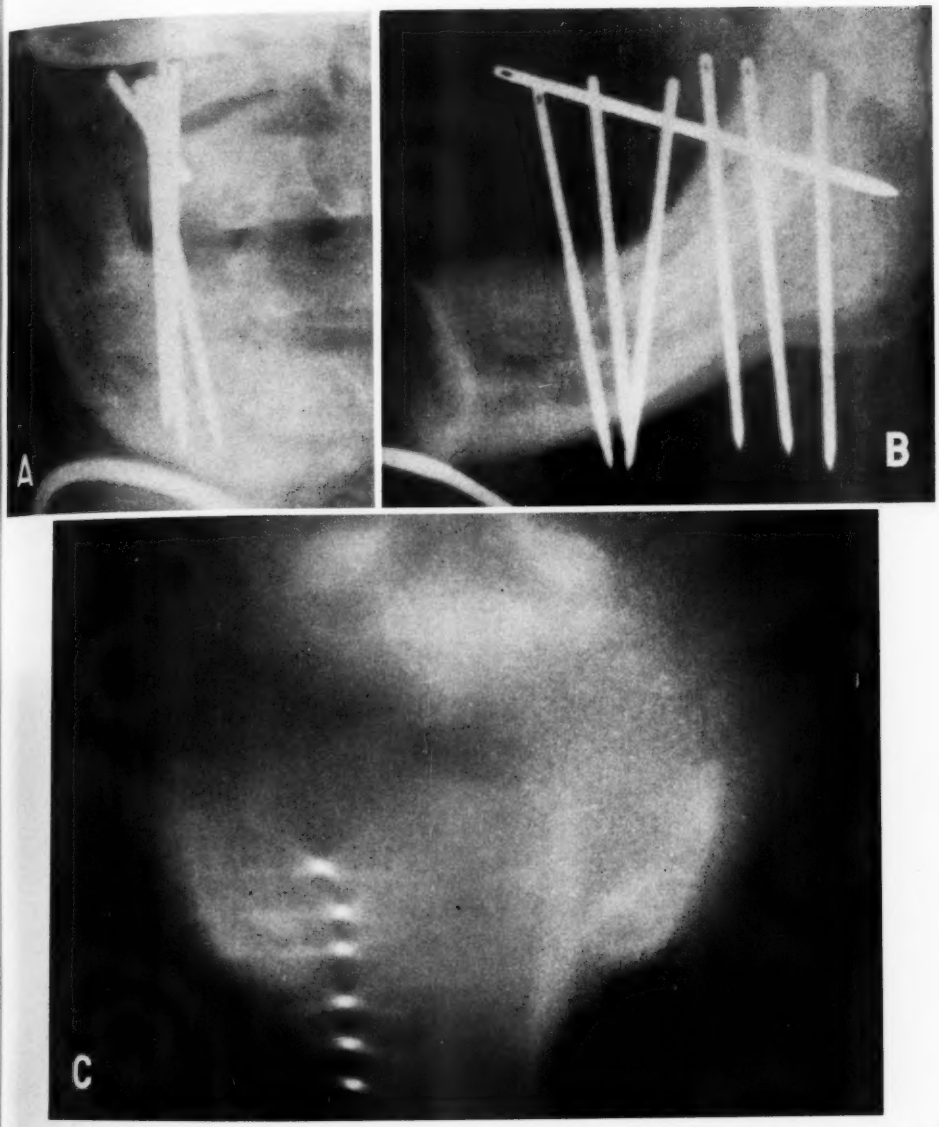


Fig. 5. Single plane implant in floor of the mouth. A. and B. Routine radiographs. C. Transverse tomogram.

routine views allows selection of the level of primary concern, usually the center of the tumor, from which accurate calculations can be made. Sequential viewing of the multiple sections provides a three-dimensional visualization of the implant and, when desired, an accurate three-dimensional reconstruction is quickly provided.

SUMMARY

Multisection transverse tomography applied to interstitial radium implants about the head and neck has been described. It allows rapid and accurate identification of radium needles and their relationships, improves the control of radiation dosage, and provides three-dimensional insight

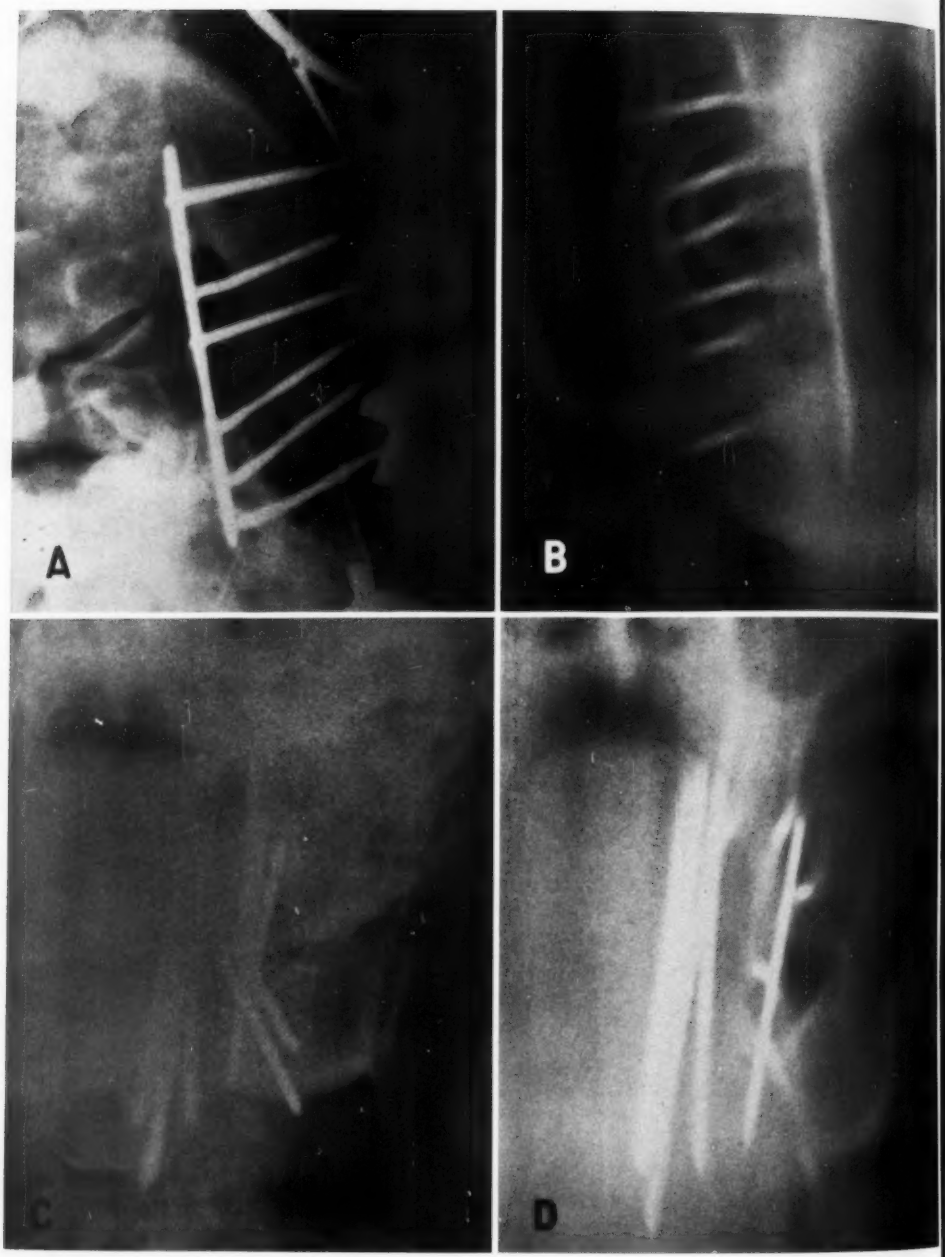


Fig. 6. Frontal tomograms, obtained with linear tube travel. A. Single plane implant in buccal mucosa. B. Tomogram. C. Double plane implant in lateral border of the tongue. D. Tomogram.
Note: The radium needles parallel to the axis of tube travel show almost equally at all levels. Usefulness of procedure depends on careful alignment and interpretation.

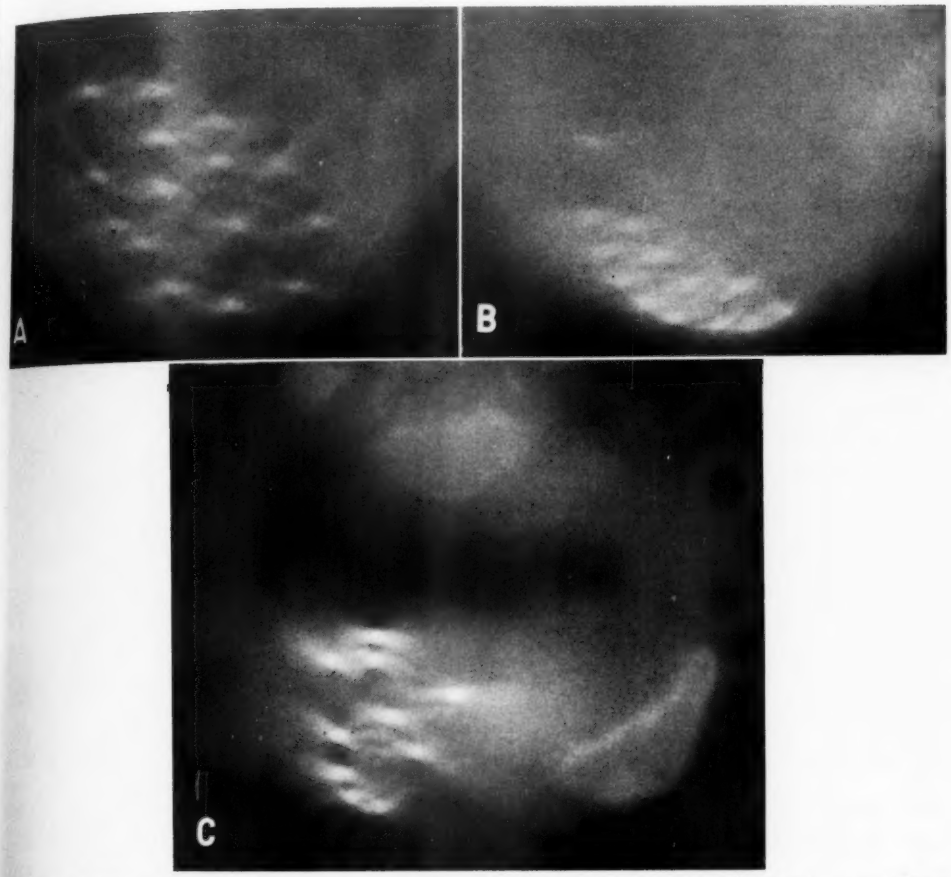


Fig. 7. A. Volume implant in tongue. B. Narrow double plane implant in floor of the mouth. C. Volume implant in recurrence in tongue; patient had had previous "Commando" procedure with hemi-mandibulectomy.

into the clinical use of interstitial radium.

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SUMMARIO IN INTERLINGUA

Tomographia Transverse Multisectional in le Calculation de Implantas de Radium

Es describite tomographia transverse multisectional in su application a implantas interstitial de radium circum le capite e le collo. Illo permitte le rapide e accurate identification de agulias de radium e lor interrelation e provide un visualisation tridimensional del uso clinic de radium interstitial.

Hypertrophic Osteoarthropathy in Children[1]

VERNON L. MEDLIN, M.D.

HYPERTROPHIC osteoarthropathy is defined as a syndrome consisting of clubbing of the digits and ossifying periostitis, primarily of the long tubular bones, occurring as the sequel of a major visceral disorder, usually intrathoracic in location.

Several publications in recent years (8, 17) have emphasized the significance of periosteal new bone formation in adults and the possible relationship of this finding to bronchogenic carcinoma. Hypertrophic osteoarthropathy is also not infrequently seen in adults in association with chronic suppurative lung disease. In patients of the pediatric age group, however, the condition has received little attention. A decade passed between the two most recently published cases (7, 9) in the American and British literature, and Caffey (2) states that the condition must be rare in this country.

TABLE I: REPORTED CASES OF HYPERTROPHIC OSTEOARTHROPATHY IN THE PEDIATRIC AGE GROUP (UP TO AGE TWELVE)

Author	Sex	Age	Primary Pathology
Whitman (18)	F	6 years	Pott's disease with tuberculous and possibly suppurative pulmonary disease
Hyman and Herrick (10)	F	2 years, 4 months	Primary disease obscure
Kennedy (11)	M	7½ months	Lung abscesses
Gottlieb *et al.* (7)	F	2 years	Pyopneumothorax
Honska *et al.* (9)	M	10 years	Ulcerative colitis
Davis (3)	M	4 years, 6 months	Empyema
Bryan (1)	M	12 years	Lung abscess

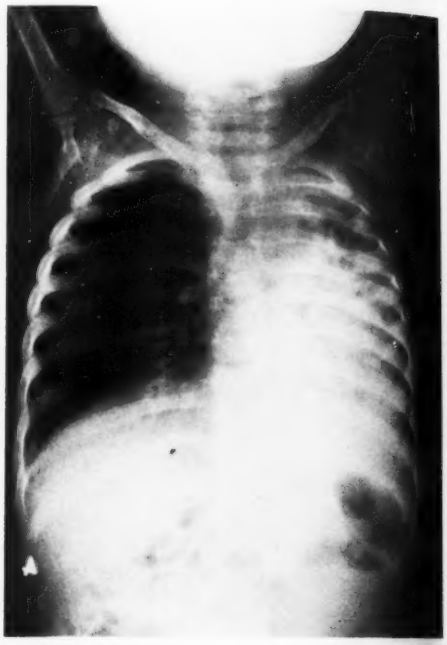

Fig. 1. Case I. Loss of all normal architecture of the left lung, with extensive consolidation and multiple cystic areas. Mediastinal shift to the left and herniation of the right lung across the midline.

A search of the American and British literature has revealed 8 case reports of hypertrophic osteoarthropathy in children up to the age of twelve. None of the cases are to be found in the radiologic literature, and only 5 (18, 10, 11, 7, 9) are accompanied by radiologic proof of the diagnosis. Two (1, 3) of the remaining 3 cases, on the basis of clinical criteria, appear to be valid instances of the condition, while the remaining case (13) is doubtful, since only digital clubbing is reported. The data on the 7 cases with periosteal changes are summarized in Table I.

Three reports of cases in the adolescent age group were found. Two of these were in fourteen-year-old boys, one associated with widespread tuberculosis (12) and the other with carcinoma of the thymus (16). The third patient was a fifteen-year-old girl with extensive tuberculosis (5).

It is proposed at this time to present 2 cases of hypertrophic osteoarthropathy in

[1] From the Department of Radiology, University of Mississippi Medical Center, Jackson, Miss. Accepted for publication in May 1959.

children seen at the University of Mississippi Medical Center.

CASE REPORTS

CASE I: A colored girl, 3 years and 10 months of age, was admitted on Sept. 26, 1958, with a history of "a cold all her life" and "sores on the body." Almost since birth upper and lower respiratory complaints had been present, characterized by rhinorrhea and cough productive of thick, green mucoid material, with episodes of fever. The sores were

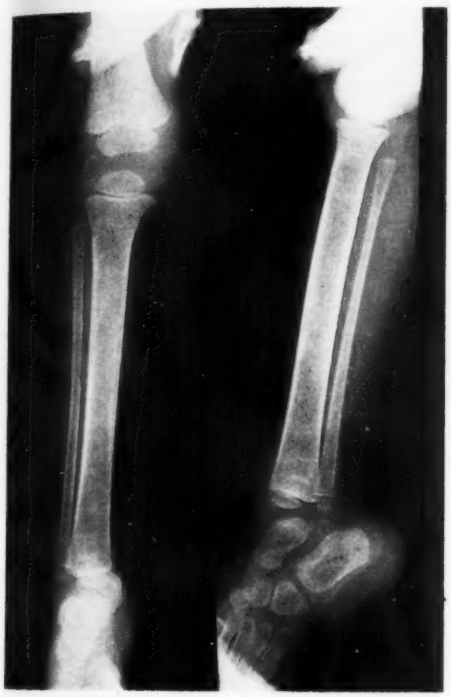

Fig. 2. Case I. Extensive periosteal new bone along the shaft of the right tibia and fibula.

described as large vesicles which ruptured and became pustular, with improvement in the winter and recrudescence in the spring and summer. The child had generally failed to thrive and was slower in development than her siblings.

On admission the temperature was 100.6°, pulse 152, respirations 36. The weight was 16 pounds 5 ounces, and the general appearance was that of a poorly developed, poorly nourished, chronically ill child. Crusted, excoriated lesions draining purulent material were seen on the extremities, trunk, face, and scalp. Physical signs of consolidation were present over the left lung field, with scattered inspiratory râles over the right lung field. Marked clubbing of the fingers and toes was noted, but there was no cyanosis.

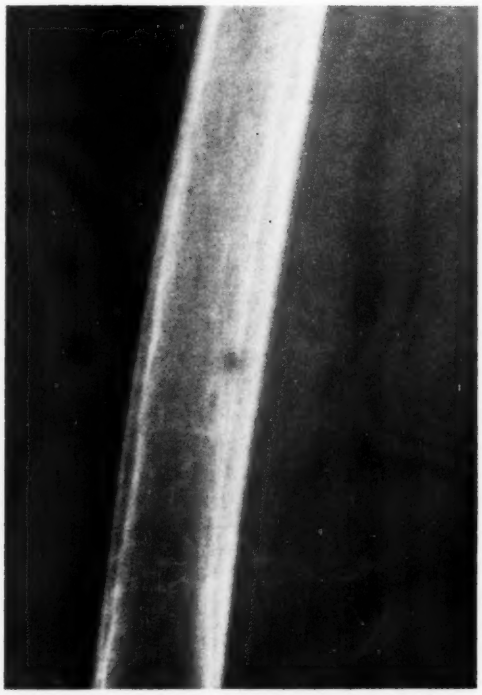

Fig. 3. Case I. A close-up view of the left femur in the mid shaft region showing to better advantage the thickness of the periosteal new bone. The bony structure is osteoporotic.

The initial clinical impressions were chronic lung disease, impetigo, and malnutrition.

Admission laboratory study revealed hemoglobin, 6.5 gm. per cent; packed cell volume 29, vol. per cent; white cell count, 12,000. The urine was reported as showing albumin 4 +, 10 to 15 white blood cells and 5 to 10 red cells per high-power field, and occasional granular casts. The serologic test for syphilis was negative, as was the sickle-cell preparation. Cultures for acid-fast bacilli and fungi were negative, only diphtheroids being recovered from the sputum. Staphylococci and streptococci were cultured from the skin lesions. PPD and histoplasmin skin tests were negative.

An admission chest film (Fig. 1) showed extensive destructive changes in the left lung field. Marked periosteal new bone was demonstrated (Figs. 2 and 3) about the shafts of the long bones of all four extremities.

Intensive therapy with antibiotics, expectorants, postural drainage, vitamins, iron, diet, and whole blood was given. The hemoglobin and hematocrit rose to 13.4 gm. per cent and 48 vol. per cent, respectively, and the urine cleared. The skin lesions responded well to routine dermatologic therapy for impetigo, and there was a weight gain of 2 pounds 3 ounces.

A bronchogram (Fig. 4) showed extensive bron-

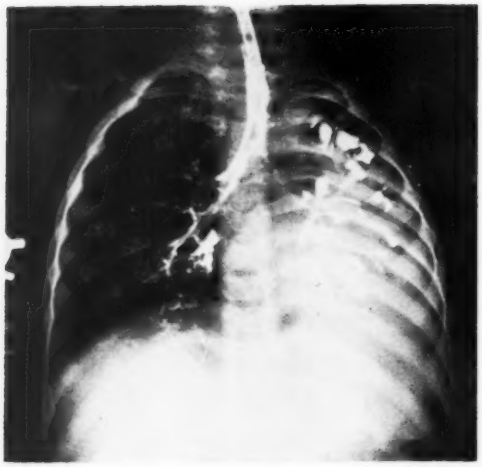

Fig. 4. Case I. Extensive cylindrical and saccular bronchiectasis on the left, with bronchiectatic cavities. The right bronchial tree is relatively normal.

chiectasis on the left. During the bronchographic study the patient suffered transitory cardiac arrest, but a normal rhythm was restored with administration of oxygen and pounding on the anterior chest wall.

On Oct. 28, 1958, a left pneumonectomy was performed. Anatomic study of the surgical specimen confirmed the radiographic finding of extensive bronchiectasis. Postoperatively the patient had copious secretions and pneumonitis developed on the right. Death occurred on the seventh postoperative day following an apparent bout of regurgitation and aspiration.

Autopsy permission was unfortunately refused by the mother.

CASE II: A 9-year-old colored male was admitted on Oct. 10, 1958, with history of "asthma" for five years. The asthmatic attacks, as described, were characterized by cough, dyspnea, orthopnea, and fever, without definite wheezing. Cough, with less marked dyspnea, was present between acute episodes. Five weeks prior to admission a severe respiratory episode developed, and the child had been confined to bed for three weeks. The cough became productive of one cup of yellow purulent sputum per day. Two days before admission the patient was seen by his local physician and a chest film revealed marked pulmonary changes. The patient was then referred to the University Medical Center.

The child was thin and debilitated, appearing acutely and chronically ill. The temperature was 101.6°, pulse 132, respirations 40, weight 50 pounds. Physical signs of consolidation were present over the left lung field and a few scattered râles were heard on the right. No cyanosis was noted, but there was clubbing of the fingers and toes. The initial clinical impression was chronic lung disease.

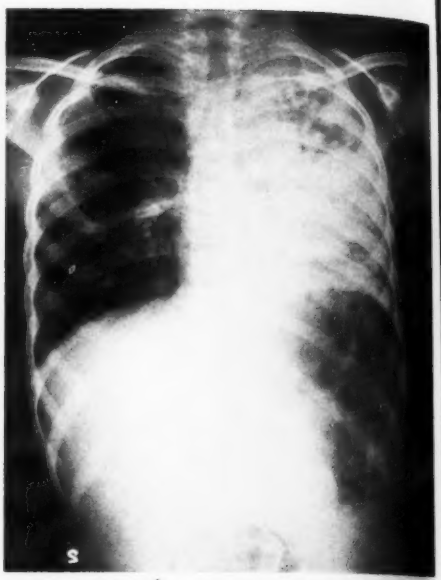

Fig. 5. Case II. Complete loss of normal pulmonary architecture on the left, with marked consolidation and multiple cystic areas. A large cystic lesion occupies much of the upper and mid lung field on the right, with a pleuritic reaction over the upper lung field on that side and mottled infiltration at the base.

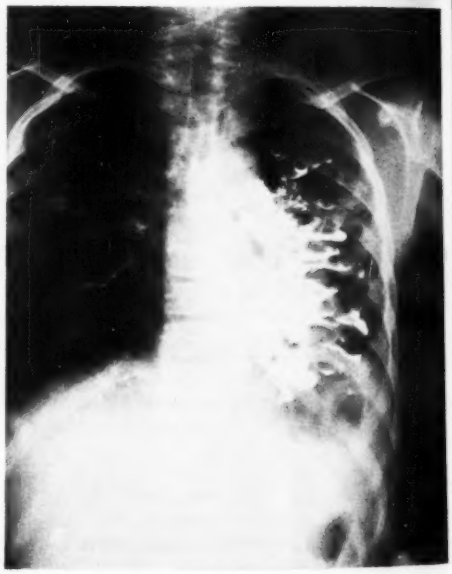

Fig. 6. Case II. Extensive bronchiectasis and bronchiectatic cavitation on the left. The consolidation on the left has cleared considerably with medical therapy. The large cystic lesion on the right is much smaller, and the pleuritic reaction has decreased. (The cystic lesion decreased further in size, but the right lung field was never completely clear prior to surgery.)

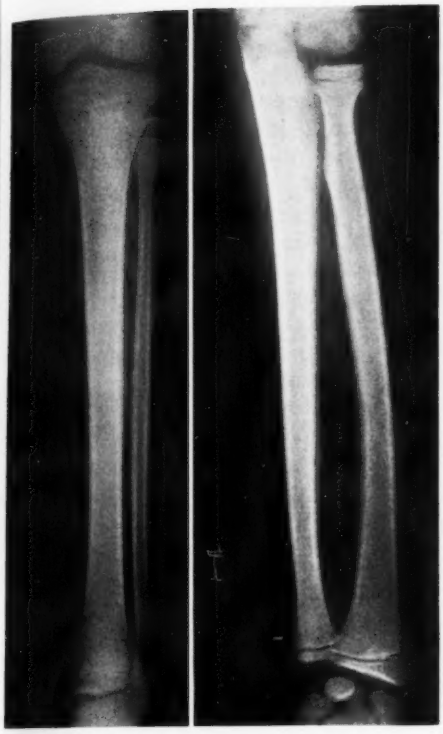

Fig. 7. Case II. Periosteal new bone, seen as a thin line about the shaft on the left tibia and fibula and the right ulna.

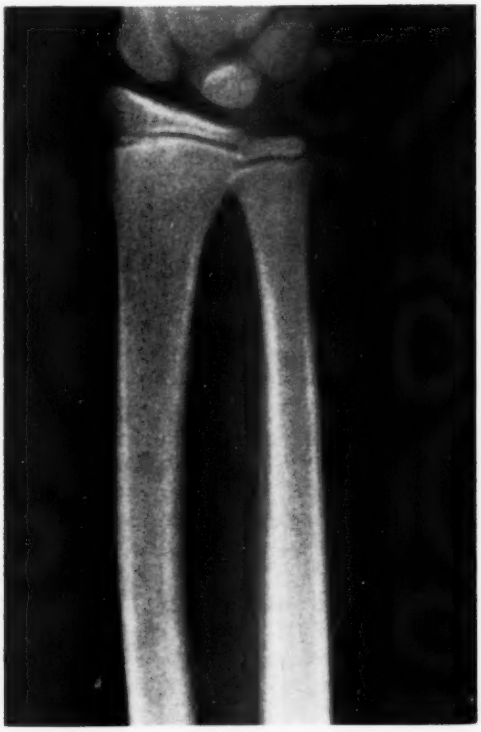

Fig. 8. Case II. Close-up view of the ulna, better demonstrating the periosteal reaction which was present in both the upper and lower extremities.

Positive laboratory findings were: hemoglobin, 8.1 gm. per cent; packed cell volume, 25 vol. per cent; white cell count, 4,500; trace of albumin in the urine. A serologic test for syphilis was negative, as was the sickle-cell preparation. Alpha hemolytic streptococci, *Neisseria*, and *Candida albicans* were cultured from the sputum. Cultures for acid-fast bacilli and for other fungi were negative, as were the PPD and histoplasmin skin tests.

The admission chest film (Fig. 5) showed a pattern not too dissimilar to the first case, with advanced disease of the left lung and some infiltration and cyst formation on the right. A bronchogram (Fig. 6) revealed extensive bronchiectasis on the left. Long-bone films showed periosteal new bone formation in the forearms and legs (Figs. 7 and 8), though the process was much less extensive than in the first case.

The same vigorous therapy as outlined for Case I was given this patient. The hemoglobin rose to 14.6 gm. per cent, the hematocrit to 42 vol. per cent, and the weight to 64 pounds.

On Dec. 5, 1958, a left pneumonectomy was performed. Anatomic study of the surgical specimen revealed widespread bronchiectasis, with chronic pneumonitis and fibrosis. The postoperative course was uneventful, and the patient was discharged on Dec. 23 to be followed in the Out-Patient Department. On subsequent visits he has been found to be doing well, with an occasional "cold" and cough productive of yellowish white sputum, one teaspoonful to one tablespoonful per day. No recurrent episodes of "asthma" have been noted, and no fever has been detectable by the mother.

On repeat long-bone films, Feb. 24, 1959, the periosteal new bone was less apparent, with partial fusion into the underlying cortex. The clubbing of the fingers remained, but was less noticeable.

RADIOGRAPHIC FINDINGS AND DIFFERENTIAL DIAGNOSIS

The radiographic findings of hypertrophic osteoarthropathy are primarily limited to the long tubular bones and are usually bilaterally symmetrical. The distal thirds of the tibia and fibula, and the radius and ulna, are usually first involved, with the femur and humerus next in frequency, and the metacarpals and metatarsals occasionally demonstrating the peri-

osteal new bone formation. The bony changes are usually more pronounced at the insertions of tendons and ligaments.

The appearance of the periosteal new bone can vary from a thin elevated line, as seen in Case II, to a marked thickening, resulting in some difficulty of differentiation from the original cortex, as shown in Case I. Osteoporosis is usually seen when thickening of the new periosteal bone is pronounced. The new bone may be as much as 6 to 8 mm. in thickness and frequently shows layers which are thought to represent response to exacerbations and remissions of the primary condition. The bony changes have been seen to disappear with cure of the primary disease (1, 14). The soft tissues of the distal phalanges appear widened from the associated clubbing.

Differential diagnosis is not very difficult. The intrathoracic or other primary disease and the associated clubbing point to the condition. Specific periostitis as seen with osteomyelitis and several of the avitaminoses is excluded by the distribution of the bony changes, along with the clinical picture and lack of clubbing. Syphilitic periostitis can be ruled out by a negative serologic test and the lack of other stigmata of congenital syphilis. The periosteal reaction seen with sickle-cell disease can be excluded by a negative sickle-cell preparation. Nonspecific periostitis, occasionally seen in chronically ill, debilitated children, presents the most difficult differential problem. It is fully realized that some question may arise as to whether the two cases reported here may not represent nonspecific periostitis rather than true hypertrophic osteoarthropathy. These cases, however, meet all the criteria, both clinical and radiologic, defined for the latter condition and outlined by Mendlowitz (14), in his definitive and extensive review on clubbing and hypertrophic osteoarthropathy.

DISCUSSION

Numerous synonyms for hypertrophic osteoarthropathy have been suggested by various authors. Occasionally the term Marie-Bamberger's disease is used, as these workers were the first to describe and differentiate the syndrome (14). The term hypertrophic pulmonary osteoarthropathy is now infrequently employed, as it has become more fully realized that the soft-tissue and periosteal changes can occur with chronic disease of organ systems other than the lungs.

There is at present unanimity of opinion that clubbing represents an early stage of the disease and that the periosteal changes are an extension of the same process. The clubbing may precede the periosteal changes by several years. In the cases reported here the interval between these manifestations is unknown, although the primary pulmonary disease had been present for years.

The pathologic changes in the bones, as reported by Gall *et al.* (6), consist initially of a thickening of the periosteum with infiltration of lymphocytes, plasma cells, and a few polymorphonuclear leukocytes. Osteoid is then laid down, becoming calcified as the inflammatory stage subsides. Subsequently the original cortex becomes osteoporotic and there is difficulty in differentiating it from the periosteal new bone. All the above changes may be seen in different portions of a single bone at the same time.

Since the original description of hypertrophic osteoarthropathy, numerous theories of etiology and pathogenesis, varying from absorption of toxins through vitamin deficiency to endocrine imbalance, have been advanced. Attempts have been made to produce the entity experimentally, but Mendlowitz and Leslie (15) appear to be the only workers who have had any success. They anastomosed the left auricle and pulmonary artery in dogs and produced the periosteal changes of hypertrophic osteoarthropathy in one animal. Mendlowitz (14) feels that increase in peripheral blood flow is, at least in part, responsible for the changes. The most recently advanced theory (4) is that the manifestations of hypertrophic osteoarthropathy are caused by a pulmonary neural reflex mediated by the vagus.

SUMMARY

Hypertrophic osteoarthropathy in children is infrequently observed. Two new cases seen at the University of Mississippi Medical Center, in patients in the pediatric age group, are reported here.

The previously published cases are briefly reviewed, and the pathology, radiologic findings, and differential diagnosis are discussed. The differentiation between hypertrophic osteoarthropathy and the nonspecific periostitis occasionally seen in chronically ill, debilitated infants and children is admittedly difficult.

It is suggested that the rarity of case reports in children may be due to an unawareness of the occurrence of the syndrome in this age group rather than to an actual low incidence.

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(Pro le summaria in interlingua, vider le pagina 427)

Roentgen Characteristics of Cavernous Hemangioma of Striated Muscle[1]

E. ROBERT HEITZMAN, JR., M.D., and JAMES B. JONES, M.D.

IN DECEMBER 1957, it was stated by Bendeck and Lichtenberg (2) that approximately 400 cases of cavernous hemangioma of striated muscle had appeared in the literature. In reviewing the series thus far reported, it is evident that great difficulty has been experienced in making a correct preoperative diagnosis of this condition. Undoubtedly, failure to think of hemangioma as a possibility is the major factor responsible, but it is also clear that the findings on the plain roentgenogram are not commonly appreciated. While the reported series show a preoperative diagnostic accuracy of up to a maximum of 46.5 per cent (8), roentgen changes were present in from 48 to 73 per cent. Certainly, if these changes had suggested the possibility of hemangioma, the diagnosis would have been made with much greater frequency. It is evident that correct preoperative recognition of the lesion is of great importance, since an unexpected encounter with the large vascular channels feeding and draining one of these tumors may present a formidable problem, particularly to those unfamiliar with this type of surgery.

The classification of tumors of blood and lymph vessels is a complicated problem and one upon which agreement is not universal. Hemangiomas may be divided broadly into capillary and cavernous types. The former are seen microscopically as a mass of newly forming capillaries with a sparse fibrous stroma, while the cavernous lesions appear as large blood-filled spaces lined by flat endothelium. Subforms of the cavernous type comprise almost all of the hemangiomas of special organs, such as the liver, intestine, bone, and muscle. Of 93 cases reported by Johnson *et al.* (8), 73 were discrete and 20 diffuse. These tumors are usually felt to be entirely benign, but Pack (11) states that malignant transformation may occur in rare instances. Matas (10) and others have reported cases of "benign metastasizing hemangiomata" but Stout (15) feels that these were actually hemangioendotheliomas from the beginning, rather than hemangiomas.

The etiology of hemangiomas is obscure. They have most commonly been considered congenital abnormalities, but the work of Andervont (1), who has produced hemangiomas with carcinogens, throws doubt on congenital factors as the sole causal mechanism.

The majority of the tumors are present at birth but may remain asymptomatic until late childhood or early adult life. Most of those which produce symptoms, however, do so before the age of thirty. They seem to be somewhat more common among females.

Hemangiomas of skeletal muscles have a predilection for sites distal to the elbow and below the knee. The most common symptoms, in order of frequency, are the presence of a mass, pain, swelling, and cosmetic change. The mass may alternately increase and decrease in size, pain often being noted with enlargement. The reason why these tumors produce pain is not well understood. The mass may enlarge and change color when the part is dependent. Pulsations and bruits are rare (5).

The diagnosis of hemangioma is dependent upon the history, physical examination, and the roentgenogram. Direct needling of the palpable mass is advocated by some as a diagnostic method.

ROENTGEN FINDINGS

Roentgen changes suggestive of hemangioma appear to be present in over half

[1] From the Departments of Radiology, State University of New York, Upstate Medical Center, and VA Hospital, Syracuse N. Y. Accepted for publication in May 1959.

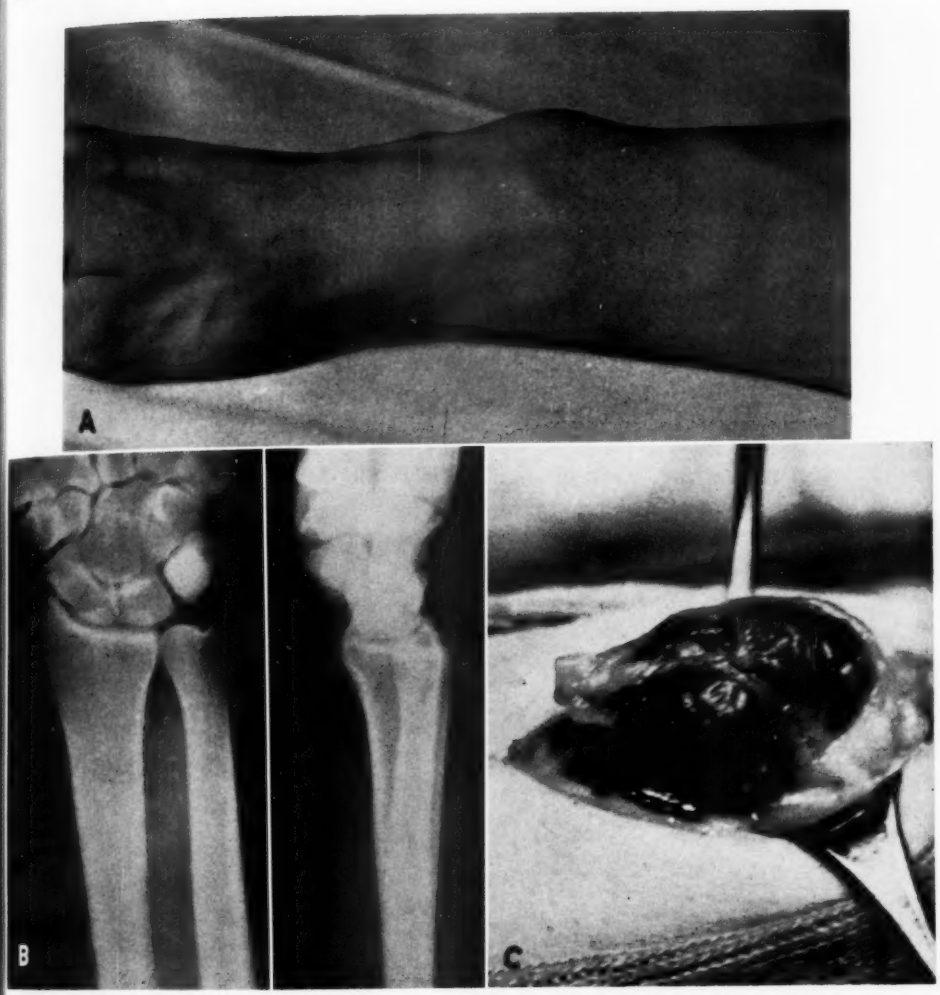

Fig. 1. A. Photograph of forearm of a young male showing a soft-tissue mass.
B. Roentgenograms of the wrist (same case as A) showing multiple round dense calcific shadows of varying size in the soft tissues. Presence of calcified phleboliths in this area, where normally no venous plexus occurs, is pathognomonic of hemangioma.
C. Photograph of the specimen at surgery showing a walnut-sized mass distended with blood.

of the cases. Phleboliths are the most commonly encountered finding, occurring in 49 per cent of the cases reported by Shallow *et al.* (14). These are seen as dense, rounded calcific masses in which a laminated structure is often identified. Fulton and Sosman (5) state that "a number of these calcified shadows in x-ray films in areas of the body where there is normally no plexus of veins is indicative of an abnormal collection of venous channels and is to all intents and purposes pathognomonic of a 'venous angioma.' "

The second most commonly encountered roentgen finding in cavernous hemangioma of skeletal muscle is calcification of the tumor. Calcium was present in 15 per cent of the cases of Jenkins and Delaney (7). It may be amorphous or may, at times, appear as grouped curvilinear shadows. In some instances, the lesion may

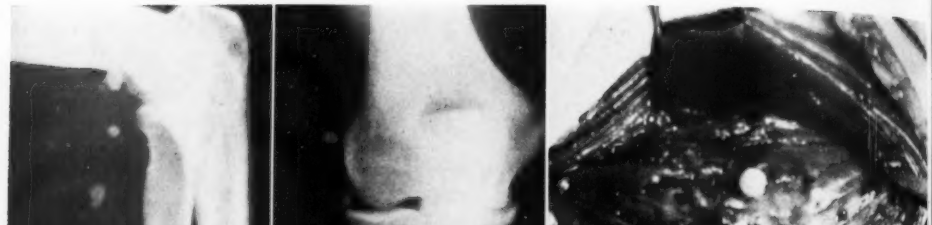

Fig. 2. A. Phleboliths in a large hemangioma adjacent to the elbow. Note the round configuration, dense structure, and radiolucent center.
B. Photograph at surgery of the hemangioma involving the belly of the extensor carpi radialis longus muscle. Note the tortuous veins over the surface of the mass and the phlebolith shelled out of its venous channel.

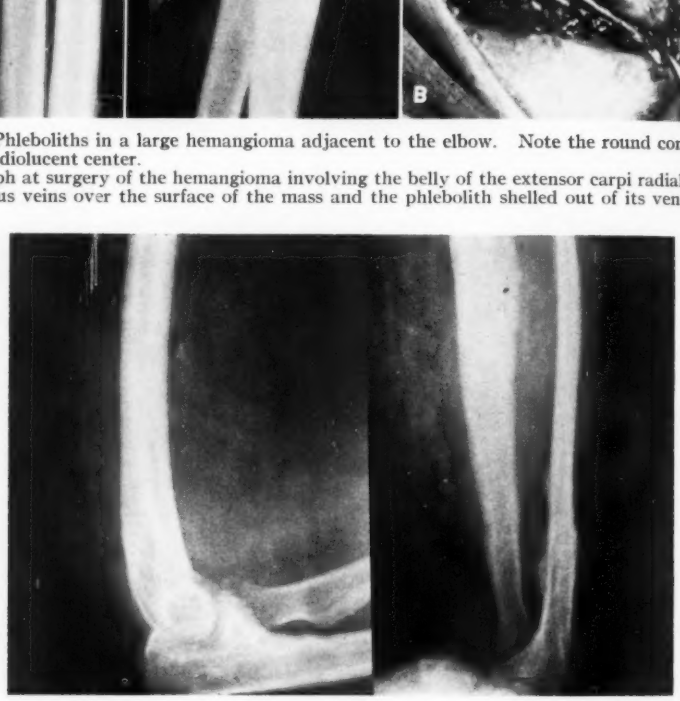

Fig. 3. Examination of the right arm of a patient with diffuse enlargement of the entire arm since birth. The bones demonstrate an irregular contour and periostitis. The irregular serpentine shadows coursing through more radiolucent fat represent abnormal blood vessels on the surface of a diffuse muscular hemangioma, later proved by biopsy.

resemble a calcified sponge. Occasionally, the density and compact nature of the calcium may suggest bone; microscopically, mature bone was identified in 2 of our cases. While the "calcified sponge" appearance is rather strongly suggestive of the diagnosis of cavernous hemangioma, nondescript calcification in the soft tissues of the arms or legs may be produced by many lesions. However, the presence of an abnormal collection of calcium in the soft tissues of the extremity of a young person, particularly if there is associated cortical thickening or cortical erosion of adjacent bone, should strongly suggest hemangioma.

Bone erosion adjacent to vascular structures, *e.g.*, aneurysm, is a well known phenomenon and is seen in some cases of striated muscle hemangioma located in close proximity to bone. In these instances erosion may be related to change

in the tumor volume as it fills and partially empties of blood.

Periosteal new bone formation occurs as a roentgen finding in a small percentage of these tumors. Such a finding, when isolated, is of course entirely nonspecific, as are osteoporosis, cortical thickening, cortical erosion, and demonstration of a mass, all of which occasionally occur secondary to adjacent cavernous hemangiomas.

In larger hemangiomas, especially those adjacent to a layer of overlying fat, the peripheral vessels may be seen as tortuous channels outlined against the more radiolucent fatty tissue.

Occasionally, hemangiomas may result in regional hypertrophy of bones and soft tissues if the epiphyses have not yet closed.

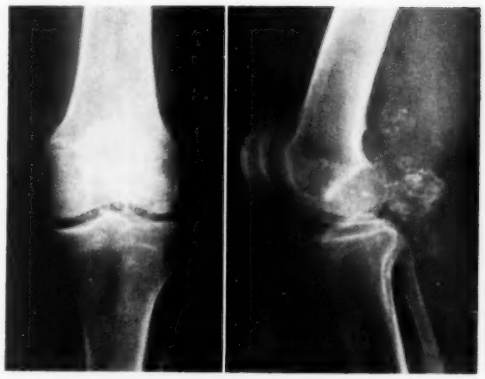

Fig. 5. Calcified chondrosarcoma. Note the similarity of the calcification in this case to that in the hemangioma shown in Fig. 4. An important point of differentiation is that, despite the rather extensive calcification present, there is no evidence of phlebolith formation.

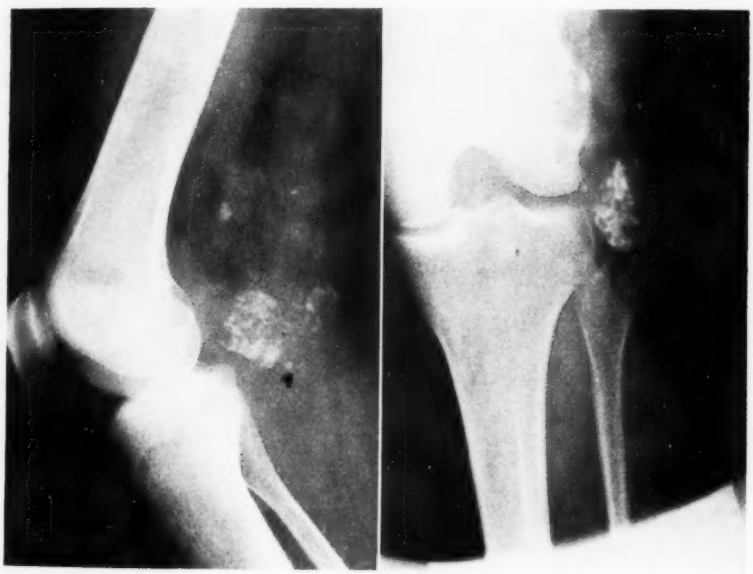

Fig. 4. Calcified soft-tissue mass presenting the appearance of a calcified sponge. This appearance is thought to be quite characteristic of hemangioma of striated muscle; diagnosis is confirmed by the rounded phlebolith designated by the arrow.

Such local gigantism is related to the increased oxygen saturation of the venous blood due to the presence of multiple congenital arteriovenous fistulas in the hemangiomas. In many infantile and juvenile hemangiomas of large size, however, the regional bones and soft tissues are normal or even hypoplastic (3).

Contrast studies of these vascular tumors are advocated by Fulton and Sosman (5), Pomeranz and Tunick (12), and others. The large vascular channels may be well demonstrated, and the sharp cut-off of the thrombosed vessels may be evident. Caffey (3) has stated that venography is the best method of determining the size and

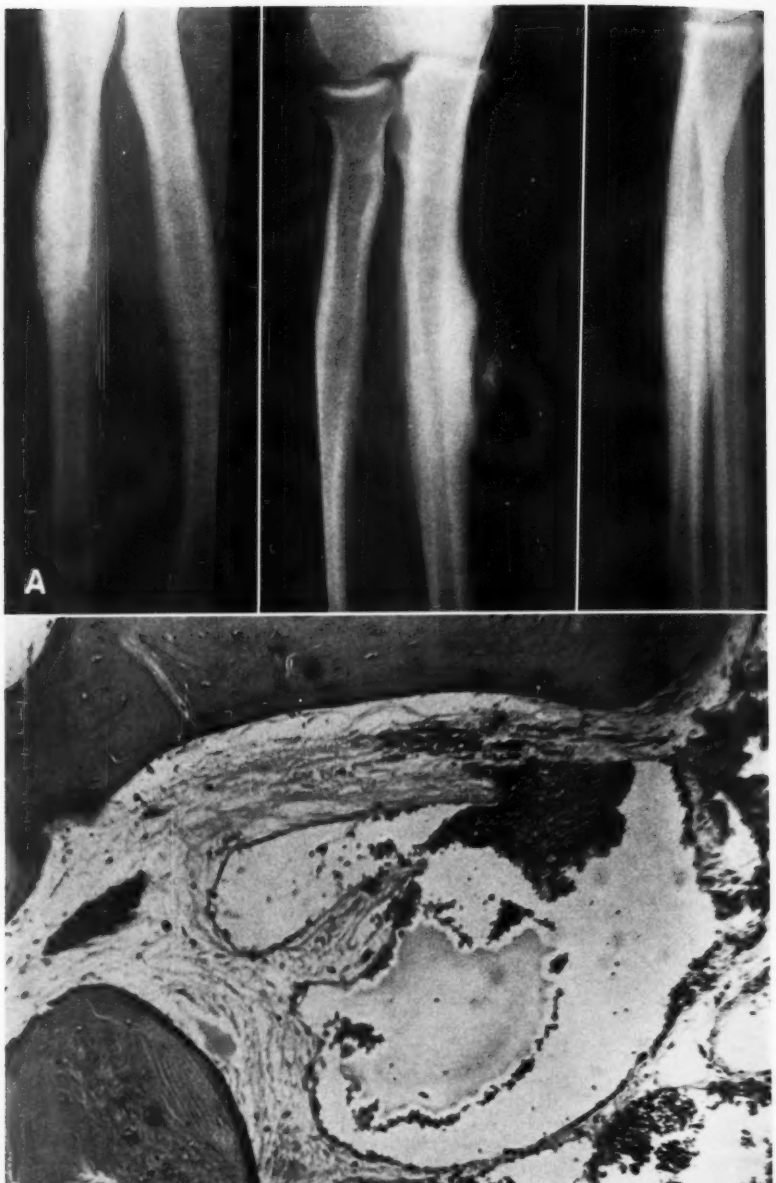

Fig. 6. A. Calcified sponge-type of calcification in the soft tissues of the forearm. There is adjacent cortical thickening with a concave peripheral margin. The combination of these two findings in an extremity of a young individual should strongly suggest the diagnosis of hemangioma.

B. Photomicrograph of the specimen. Note the large dilated blood-filled spaces and the mature bone which formed a portion of the tumor.

morphology of the arteriovenous fistulas in the larger hemangiomas. Venography was done in only 2 of our cases, both small tumors in which the large number of phleboliths indicated the obliteration of many of the venous channels. No true abnormal vascularity was demonstrated, although there was obvious displacement of veins about a mass.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis of these lesions, a typical history of recurrent pain, swelling, and cosmetic change is extremely helpful and should lead to a presumptive diagnosis of hemangioma.

As has been stated, the presence of phleboliths in any area where no venous plexus normally occurs is pathognomonic of a venous angioma. Similarly, the outline of tortuous vascular channels against overlying fat is indicative of a tumor made up, at least in part, by abnormal veins.

When calcification only is seen in the soft tissues of the extremities, a wide variety of conditions enter into the differential diagnosis. Myositis ossificans usually presents a streaky type of calcification unlike that occurring in hemangioma. Interstitial calcinosis, as a rule, involves skin and subcutaneous fat early. Later, when muscles are affected, the disease is usually readily distinguished. Parasites, when calcified, may frequently be recognized by a characteristic shape and by their often generalized distribution. Two cases of calcified neurofibromas, described by Holt, are discussed by Caffey (3). Multiple bone lesions were also present in these patients. In addition, calcified hematoma or more rarely chronic abscess, granuloma, aneurysm, dermoid, etc., may be considered.

Local gigantism is found with large tumors of lymphatic and neurogenic origin as well as with hemangioma.

If cortical thickening is the sole roentgen abnormality, osteoid osteoma could be considered in the differential diagnosis. In this disease a nidus is often visible and the peripheral margin is usually convex, while in hemangioma it is likely to be concave.

Fig. 7. Examination of the forearm in a case of cavernous hemangioma of striated muscle. There is an irregularity of the cortex of the distal radius with a somewhat concave peripheral border. While such a finding is rather nonspecific, in a young individual with a typical story a diagnosis of hemangioma of striated muscle may be made with some certainty.

Of the malignant lesions to be differentiated, osteogenic sarcoma often produces new bone in adjacent soft tissues, but the nature of the calcification, the periosteal reaction, and bone destruction should point to a malignant process. Chondrosarcoma may present a distinct problem if the roentgen manifestation is primarily a soft-tissue mass with calcium. Careful evaluation of the calcification may uncover phleboliths in the hemangioma. Hale (6) states that synovioma may be strongly suspected when "a soft tissue mass in a joint or near a joint is lobulated and contains a fine speckled type of calcium which is laid down in small rounded masses irregularly arranged." Such a lesion may be indistinguishable from hemangioma at

or near a joint. Again, demonstration of phleboliths may distinguish the hemangioma, as may a long history of recurrent pain, swelling, or cosmetic change. Venography may be helpful in these instances.

TREATMENT

While various methods, including direct injection of sclerosing solutions, electrocoagulation, roentgen and radium therapy, have been advocated for the management of hemangiomas of striated muscle, surgery remains the treatment of choice.

SUMMARY

Hemangiomas of striated muscle are not rare and are often misdiagnosed. Since roentgen changes suggestive of the diagnosis are found in as high as 73 per cent of cases, a review of these changes has been undertaken to emphasize the importance of radiological examination in these lesions.

NOTE: The authors express their appreciation to Drs. Stephen Bastable and Richard Gale of Syracuse, N. Y., for permission to reproduce the roentgenograms shown in Figure 4.

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SUMMARIO IN INTERLINGUA

Characteristicas Roentgenoscopic de Hemangioma Cavernose de Musculo Striate

Hemangiomas de musculo striate non es rar. Illos ha un predilection pro sitos distal con respecto al cubito e infra le genu. Ben que illos es usualmente presente al momento del nascentia, il occurre que illos produce symptomas solmente plus tarde in le curso del pueritia o del juvene etate (ante trenta annos). Le presentia de un massa, de dolores, de tumescentia, e de un alteration cosmetic es le plus commun constatationes clinic.

Suggestive alterationes roentgenoscopic es presente in usque a 73 pro cento del casos. Istos include phlebolithos, calcification del tumor, erosion de osso, e a vices neoformationes periosteal de osso. In le lesiones de dimensiones major, specialmente in tales que se trova proxime a un

strato de grassia supra-jacente, le vasos peripheric pote esser vidite como canales tortuose que se delinea per contrasto con le plus radiolucente tissu grasse.

Le presentia de un collection anormal de calcium in le tissus molle del extremitates de un juvene subjecto, specialmente si illo es associate con spissification cortical o erosion cortical in osso adjacente, es fortemente suggestive de hemangioma.

SUMMARIO IN INTERLINGUA

Osteoarthropathia Hypertrophic in Patientes Pediatric

(*Pagina 414*)

Osteoarthropathia hypertrophic es un syndrome que consiste de formation de digitos hippocratic e de periostitis ossificante primarimente in le longe ossos tubular, occurrente como le sequella de un major disordine visceral que es usualmente sed non invariabilemente thoracic. Le condition ha essite reportate solmente in rar casos in le gruppo de etate pediatric (usque a dece-duo annos de etate). Octo tal casos esseva trovate in le litteratura american e britannic, e 2 casos additional es presentate. Le duo juveniles habeva ambes un longe historia de symptomas respiratori, e in ambes il esseva constatate al operation que illes habeva extense grados de bronchiectase.

Le formation de digitos hippocratic es generalmente considerate como pertinente al precoce stadios del morbo, durante que le alterationes periosteal es reguardate como un extension del mesme processo. In su apparentia radiographic, le nove osso periosteal pote variar inter un tenue linea elevate e un marcate spissification que es difficile a differentiar ab le cortice del osso. Osteoporosis pote esser associate con le plus marcate spissification del periosteo.

Le plus grande difficultate in le diagnose differential es representate per le periostitis nonspecific que es vidite occasionalmente in infantes e juveniles qui es chronicamente malade e debilitate.

Disseminated Lipogranulomatosis

Report of a Case[1]

GUNTER SCHULTZE, M.D., and ERICH K. LANG, M.D.

In 1947 Sidney Farber (1) observed an apparently new disease entity in an infant fourteen months of age, which he termed "disseminated lipogranulomatosis." This, he suggested, might represent a bridge between two apparently etiologically distinct groups of lipid metabolic disorders which he defined as: (*a*) true metabolic disorders, including Gaucher's disease, Niemann-Pick's disease, and Tay-Sachs' disease and (*b*) entities not believed to be primarily metabolic but rather inflammatory in the broad sense, and characterized by initially granulomatous lesions which subsequently undergo partial lipid replacement. This latter group includes Hand-Schüller-Christian disease, eosinophilic granuloma, and Letterer-Siwe's disease, all of which are now considered variations of a similar underlying process.

Subsequently Farber investigated 2 further examples (2). The 3 cases presented very similar bizarre clinical and pathological findings, which were also noted in the case to be reported here.

CASE REPORT

G. R. C., a 15-month-old Caucasian male, was admitted to The Johns Hopkins Hospital on May 22, 1957, for diagnostic evaluation. The child was born in a military camp in Japan and was considered to be full-term and normal. The family history, gestation, and neonatal periods were unremarkable. At the age of three months, feeding difficulties, anorexia, projectile vomiting, marked swelling of the wrists, and a peculiar hoarse cry, as well as a low-grade fever, were noted. Treatment with antibiotics and oxygen at the local military hospital resulted in some clinical improvement. Subsequently, marked respiratory difficulty developed and the baby was readmitted to the hospital on several occasions. Bronchoscopy revealed a "fibroma of the left vocal cord." Because of respiratory distress, a tracheotomy was performed. The child was later transferred to the Walter Reed Army Hospital for an intensive diagnostic study. At that time swellings of the joints of the fingers, hands, elbows, wrists, and knees were noted. Extensive laboratory studies were within normal limits except for an increased creatine output. A therapeutic trial of cortisone was unsuccessful, and a tentative diagnosis of arthrogryposis was made.

Physical examination at the time of admission to The Johns Hopkins Hospital revealed a small infant who exhibited marked weakness and lack of voluntary motion. The skin showed a pale yellow color without evidence of frank jaundice. All peripheral joints were grossly deformed by large, knotty, periarticular masses with a rather firm and wooden feeling, as well as by multiple flexion contractures. The joints, however, did not appear to be tender or warm, or to show any signs of inflammation. An extensive firm, knotty mass was also noted in the subcutaneous tissue of the paraspinal area, extending from about D-9 through L-3. Further positive physical findings were an extremely high palatine arch, a narrow pharynx, and a protuberant abdomen. The liver was palpable and enlarged, presenting three finger breadths below the right costal margin. The spleen was not felt. The heart and lungs appeared to be normal. The nervous system was unremarkable.

Laboratory Data: The pertinent abnormal laboratory findings included a white blood cell count of 18,900, with a normal differential count; hemoglobin 9.3 gm.; hematocrit 35 per cent; corrected sedimentation rate 26; mucoprotein fraction 14.6 mg. per cent (the normal value in this hospital is 3 to 4 mg. per cent); total serum lipids 1,226 gm. per cent; urine creatine 23.2 mg. per cent; urine creatinine 20 mg. per cent. Serial paper electrophoretic patterns showed a slight decrease in the serum alpha-2 and beta-globulin fractions. Serum transaminase, C-reactive protein, antistreptolysin 0-titer, alkaline and acid phosphatase, uric acid, total cholesterol, blood sugar, serum electrolytes, and spinal fluid, as well as throat and blood cultures, were normal.

Roentgen Findings (*Figs. 1 and 2*): Roentgenograms of the affected joints demonstrated marked swelling and distention of the joint capsule by a substance of soft-tissue density, resulting in subluxation of one hip and one elbow joint. This articular distention is particularly well shown in the region of the interphalangeal joints of the right thumb (Fig. 1). An erosion of the distal portion of the right ulna, caused by the pressure of the adjacent

[1] From the Department of Radiology, The Johns Hopkins Hospital, Baltimore, Md. Accepted for publication in March 1959.

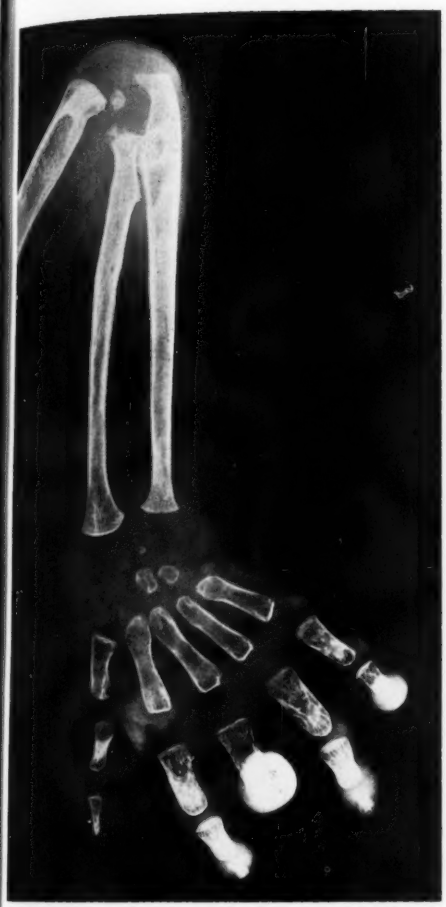

Fig. 1. Roentgenogram of the right forearm demonstrating marked capsular distention of elbow, wrist, and interphalangeal joints by a substance of soft-tissue density. Note the subluxation of the elbow joint and grotesque deformity of the soft tissues of the right thumb.

soft-tissue masses, is also present. The peripheral bones are demineralized, probably secondary to disuse or previous massive cortisone therapy. The soft-tissue and fascial planes are well maintained and, while there is a generalized decrease of muscle tissue, no radiolucent striations suggestive of fatty replacement of the muscles are observed. Apart from the soft-tissue and bony changes the admission chest film was within normal limits.

Pathologic Findings: Biopsies of the left wrist and of the paraspinal area showed infiltrations of macrophage-like cells with pink cytoplasm. Special stains revealed rare vacuolization and demonstrated a lipid material which was not doubly refractile (Fig. 3). The pathologic changes were limited to nodule-like lesions with mononuclear cell infiltration, foam cells, and macrophage-like cells surrounded by dense collagen. The clumping of the cell aggregates is not unlike that seen in a rheumatoid nodule.

DISCUSSION

The striking roentgenographic feature of this condition is the extensive alteration of all peripheral joints, manifested predominantly by marked distention of the joint capsules by a substance of soft-tissue density which sometimes may cause subluxation. Juxta-articular erosion of the osseous structures may also occur and seems to be caused by pressure of the periarticular soft-tissue masses. The erosions

Fig. 2. The knee and ankle, as well as the interphalangeal joints, show capsular distention. The soft-tissue planes and arrangement of muscle bundles are maintained.

are produced by a rubbery, firm tissue encasing the articular cartilage in the form of a pannus, which occasionally thickens to form a nodule. Sections of this tissue include mononuclear cells, foam cells, and macrophages surrounding an area of hyaline or collagen degeneration. Apart from the foam cells, the patterns may simulate that seen in rheumatoid arthritis.

Farber isolated a lipoglycoprotein fraction from the granulomatous lesions of his cases which he considered biochemically characteristic of this condition. The substance is chemically different from the lipids found in Niemann-Pick's disease and in Gaucher's disease, although pathologically lipogranulomatosis has many features in common with Niemann-Pick's disease, Tay-Sachs' disease, and Hurler-Pfaundler disease. However, the generalized systemic involvement also readily differentiates it from the heredodegenerative disease group, as in the case reported here. Hand-Schüller-Christian disease, and eosinophilic granuloma are not difficult to differentiate roentgenographically from disseminated lipogranulomatosis. These entities show characteristically no involvement of the joints but may often present "punched out" lesions, a finding which has not been encountered in disseminated lipogranulomatosis.

The clinical picture of disseminated lipogranulomatosis is distinguished by its unique and uniform pattern. The early onset of the generalized joint involvement, characterized by essentially painless swelling of the joints without marked inflammatory change, a hoarse cry caused by fixation of the laryngeal cartilage by granulomatous tissue, early alternating febrile and afebrile periods, and ultimate rapid deterioration secondary to pulmonary and central nervous system involvement were encountered in all four of the cases reported to date. Similar joint changes may be found in rheumatoid arthritis. However, this disease as well as true Still's disease

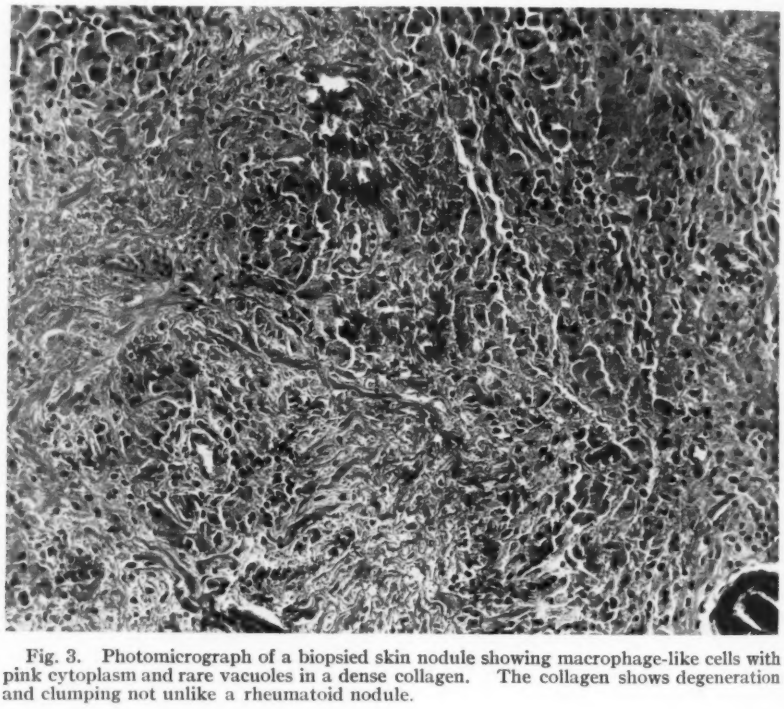

Fig. 3. Photomicrograph of a biopsied skin nodule showing macrophage-like cells with pink cytoplasm and rare vacuoles in a dense collagen. The collagen shows degeneration and clumping not unlike a rheumatoid nodule.

has not been observed in so early an age group. Moreover, rheumatoid arthritis exhibits inflammatory changes in association with painful swelling of the joints. Arthrogryposis is not likely to give difficulty in differentiation, since it is primarily a failure of muscular development with no significant joint pathology.

SUMMARY

A case of disseminated lipogranulomatosis is presented. The characteristic roentgen changes, consisting of marked capsular distention of all peripheral joints by a substance of soft-tissue density and occasional erosion of the bone by nodules of the same tissue elements are described. The pathological and clinical features of the disease are briefly discussed.

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SUMMARIO IN INTERLINGUA

Lipogranulomatosis Disseminate: Reporto de Un Caso

Lipogranulomatosis disseminate esseva primo describite como un entitate pathologic in 1947 per Farber qui suggereva que illo representava possibilemente un ponte inter duo gruppos de disordines metabolic de lipido que pareva esser etiologicamente distincte, i.e., de un latere, ver disturbationes metabolic como morbo de Gaucher, morbo de Niemann-Pick, e morbo de Tay-Sachs e, del altere latere, conditiones de natura primarimente inflammatori con alterationes subsequente de lipido, como morbo de Hand-Schüller-Christian, granuloma eosinophilic, e morbo de Letterer-Siwe.

Farber reportava 3 casos de iste condition. Es hic reportate un caso additional. Le patiente esseva un infante de dececinque menses de etate.

Characteristicamente le constatationes roentgenologic consiste in un marcate distension capsular de omne le articulationes peripheric per un substantia del densitate de tissu molle e occasionalmente in un erosion del osso per nodulos del mesme elementos tissular. Sectiones de iste tissu revela cellulas mononucleari, cellulas spongiose, e macrophagos circumdante un area de degeneration hyalin o collagenic.

Cholesterolosis[1]

CHRISTIAN V. CIMMINO, M.D., F.F.R.[2]

THE PURPOSE of the present paper is fourfold: to furnish some background material on cholesterolosis for the radiologist; to review briefly the radiologic diagnosis of cholesterolosis; to offer evidence that the cholesterol polyp may be a temporary, "pre-stone" state; to reaffirm the opinion that cholesterolosis, as suggested by the polyp, is an adequate indication for removal of the gallbladder.

TABLE I: RADIOLOGICAL FINDINGS IN FIVE CASES OF CHOLESTEROLOSIS

Patient	Number of Polyps Visualized	Visualized in— Pre-Fat Film	Visualized in— Post-Fat Film	Concentration	Size (mm.)	Location (third of gallbladder)	Irritability
1. U. B.	2	Yes	Yes	Excellent	2	Middle	No
2. M. P.	1	Yes	Yes	Excellent	5	Middle	No
3. E. W.	1	No	Yes	Excellent	5	Upper	Yes
4. E. M.	1	Yes	Yes	Excellent	2	Lower	Yes
5. E. C.	1	No	Yes	Excellent	3	Upper	No

BACKGROUND MATERIAL

Some 20 per cent of all surgically removed gallbladders show cholesterolosis of some degree, a condition characterized microscopically by deposits of cholesterol ester, both free and within macrophages (foam cells) in the subepithelial tissues. Grossly, these lipid accumulations appear as yellow foci of varying size, not unlike the yellow seeds of the strawberry, whence its designation "strawberry gallbladder." At times, the lipid deposits tend to be focal, and the massive accumulation within a fold forms a polypoid or papillomatous structure projecting into the gallbladder lumen, preserving its contact with the wall by a tenuous mucosal stalk.

Cholesterol metabolism in relation to the gallbladder is poorly understood. It is probably true that the level in the bile reflects that in the blood, and that cholesterol is maintained in solution with the help of the bile acids. It is still not agreed upon whether the gallbladder excretes cholesterol or absorbs it, or both, depending upon the relative levels in the blood and in the bile.

There are probably two factors involved in the production of cholesterolosis: (*a*) inflammation, usually of low intensity; (*b*) elevated bile cholesterol. Some say that the first factor need not always be present. The condition is commonly associated with multiple, small, pure cholesterol stones; less commonly, with the polypoid or papillomatous excrescences described above. It is most probable that the delicate stalks of the latter formations can break, thus producing a nidus for stone formation leading to symptoms as a result of extrusion of the mass down the biliary tract. Uncomplicated cholesterolosis is said to be without symptoms, but these may be produced by associated cholecystitis and cholelithiasis, as well as by the passage of the pedunculated lipid structures described above.

RADIOLOGIC DIAGNOSIS

Table I summarizes the radiologic findings in 5 surgically proved cases. Inspection allows several comments:

1. Most commonly, only a single filling defect was noted, but as many as six have been observed (1). Although only one may be apparent radiologically, multiple polyps are frequently found in the surgical specimen (see Table II).

[1] Accepted for publication in April 1959.

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TABLE II: CLINICAL AND PATHOLOGIC FINDINGS IN FIVE CASES OF CHOLESTEROLOSIS

Patient	Age	Race	Sex	Duration of Symptoms	Symptoms	Surgical Pathology	Duration of Follow-Up	Results
1. U. B.	36	W	F	18 mo.	Indigestion, RUQ pain, bloating	Cholesterol polyps, chronic cholecystitis	3 yr.	Well
2. M. P.	47	W	F	"Some time"	Gas, occasional indigestion, soreness in RUQ	Cholesterol polyp	6 mo.	Well
3. E. W.	42	W	F	"Indefinite"	Mild indigestion	2 cholesterol polyps, minimal chronic cholecystitis	1 yr.	Well
4. E. M.	45	W	F	8 mo.	Indigestion, belching and nausea. Later, typical colic	"Strawberry" gallbladder; 21 soft, yellow stones, 2–4 mm. No polyps. Chronic cholecystitis	8 mo.	Well
5. E. C.	41	W	F	1 yr.	Indigestion and typical attacks of colic	Several cholesterol polyps 2–4 mm. Several black granules in bile barely strainable with surgical gauze. Chronic cholecystitis	1 yr.	Well (of gallbladder complaints)

2. A post-fat film was required to demonstrate the filling defect in 2 of the 5 patients. This is in striking contrast to the relatively slight assistance given by the fatty meal in an unselected series of gallbladder examinations (2). The reason for this difference lies in the fact that in any unselected series of gallbladder examinations polyps are greatly outnumbered by stones, the demonstration of which is largely independent of the post-fat study (2).

3. The concentration of the opaque material (Telepaque) was excellent in every patient. This has been considered characteristic of cholesterolosis, but it is likely that the concentration depends upon the extent of associated cholecystitis. When this is minimal, there is no significant departure of concentration from the normal.

4. The largest filling defect in the present series measured 5 mm. A larger defect might suggest a cancer (3).

5. Although I recall no cholesterol polyp in the *extreme* fundus, the polyps in the present series occurred in each of the thirds of the gallbladder. It will be noted that those occurring in the upper third (patients 3 and 5) required the fatty meal for demonstration (2).

6. The opacified gallbladder at times shows a marked indentation or incisura in its contour (Fig. 2) that may mimic a large intrinsic filling defect (4). Every radiologist has seen such an appearance and has glided over the finding as representing extrinsic pressure by an adjacent viscus or, intuitively, as normal but unexplained. Andrén and Theander (5) were able to correlate this phenomenon with age and sex, showing its predominance in women in the "gallbladder age" in a series of 1,351 examinations with iopanoic acid (Telepaque). They offer the ingenious explanation that the "defect" represents an eccentric contraction of the gallbladder due to irritation by the contrast medium in a group prone to gallbladder disease (5). The incidence of irritability in the present small group is probably not statistically different from that in the same age and sex group with no abnormalities. Larger series may well show a significant difference if Andrén and Theander's thesis is correct.

THE CHOLESTEROL POLYP AS A TEMPORARY "PRE-STONE" STATE

That cholesterolosis is a factor in the production of gallstones has been widely held. Patient E. M. would appear to demonstrate such a sequence. Initially, she complained of "indigestion, belching, and nausea." Figure 1 demonstrates a fixed filling defect with no stones. Later, intermittent attacks of typical colic with epigastric and right upper quadrant pain

Fig. 1. Patient E. M. Constant fixed filling defect. Other exposures show the upper reaches of the gallbladder to be normal.

radiating to the back supervened, requiring opiates for relief. A second gallbladder examination (Fig. 2), six months after the first, shows several stones but with no filling defect, despite intensive efforts to demonstrate this. Examination of the excised gallbladder confirmed the presence of stones and diffuse cholesterolosis but showed no excrescences of any kind. The filling defect so easily and constantly demonstrated on the first examination must have been a cholesterol polyp that had regressed or formed a nidus for stone. It is tempting to equate the change in symptoms from simple indigestion to typical colic with the transition from cholesterolosis without stones to cholesterolosis with stones.

CHOLESTEROLOSIS AS AN INDICATION FOR CHOLECYSTECTOMY

Cholesterolosis (as manifested roentgenologically by the cholesterol polyp) is an adequate indication for removal of the gallbladder. Surgical excesses upon the gallbladder over the years have resulted in a restriction of the operative indications coincident with the development of dependable radiologic diagnosis. Chronic cholecystitis has not been an indication, probably because no objective test has existed for its diagnosis. The high development of the radiologic exploration of the gallbladder now allows a reasonably dependable diagnosis of the polypoid variety of cholesterolosis which should be included among the adequate indications for gallbladder surgery. The radiologic diagnosis of cholesterolosis probably is more certain in the presence of multiple

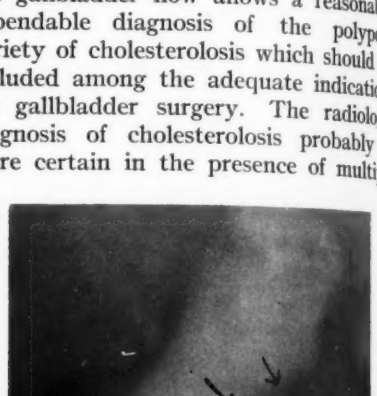

Fig. 2. Patient E. M. Six months after Fig. 1. Numerous small stones in infundibulum. Their high level of flotation indicates a low specific gravity. That of pure cholesterol is barely higher than water. Arrows indicate the eccentric contractions of Andrén and Theander. Exposures with or without these contractions fail to show the fixed filling defect of Fig. 1.

defects, but the surgical indication still exists when the defect is single, lest a premalignant or frankly malignant lesion be missed (3). The author must take exception to the opinion expressed by the late Dr. B. R. Kirklin, that "at no time did we feel that papillomas were an indication for surgery, . . ." (6).

The records of patients with cholesterol polyps who have been operated upon at this suburban hospital within the last three years and have had satisfactory clinical follow-up are summarized in Table II. It is to be noted that all were white women (about 20 per cent of our patient population is Negro). All fell within the decade limited by thirty-six and forty-seven years. This is early in the natural history of

biliary tract disease, as is further demonstrated by the relatively short duration of symptoms. In one patient stones developed during the period of observation. All have been followed from three years to six months, and all are free of symptoms.

A very practical outcome of my present and previous studies of the gallbladder is represented by the following conclusion: A patient with "indigestion," especially a white woman in the fourth or fifth decade, should not be radiologically abandoned after a single negative gallbladder study, not only because demonstration of small defects may be whimsical, dependent upon a narrow range of optimal technical factors (7), but also because cholesterolosis, a pathologic, "pre-stone" state, may be radiologically silent if there are no associated stones or polyps, or if the polyps are too small for radiologic visualization. Passage of time may allow the development of stone or polyp or both, with successful radiologic demonstration.

SUMMARY AND CONCLUSIONS

A rational, probable, radiologic diagnosis of cholesterolosis may be offered when there are fixed filling defects in the well functioning gallbladder. A focal accumulation may disappear, either by severance or involution. Cholesterolosis is an adequate indication for removal of the gallbladder. The "cholesterolosis suspect," especially the white woman in the fourth or fifth decade, should have the fatty meal as part of her radiologic exploration, especially when the density of the contrast medium in the proximal reaches of the gallbladder is suboptimal. She should not be abandoned radiologically after the first normal study but should be followed at intervals of several months if symptoms of indigestion persist.

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SUMMARIO IN INTERLINGUA

Cholesterolosis

Le diagnose radiologic de cholesterolosis pote esser formulate con satisfacentemente alte grados de definitivitate quando fixe defectos de replenation es demonstrate in un ben functionante vesica biliari. Accumulationes de lipido, non dissimile al jalne semines del fraga, ha resultate in que le condition es designate a vices como "cholecyste fraga." Accumulationes focal pote occurrer, sed istos pote disparer (1) per le separation del tenue stirpe mucosal que attacha los al pariete del vesica biliari o (2) per involution.

Cholesterolosis es un adequate indication pro le ablation del vesica biliari. Le patiente suspecte de cholesterolosis, specialmente si il se tracta de un femina de racia blanc in le quarte o quinte decennio de su vita, deberea reciper un repasto grasse como parte del exploration radiologic, super toto quando le densitate del substantia de contrasto in le areas proximal del vesica biliari es minus que optimal. Un tal patiente non deberea esser abandonate radiologicamente post le prime studio con resultatos normal sed deberea esser tenite sub observation a intervallos de plure menses si le symptomas persiste.

A Double-Blind Study of Oral Cholecystographic Media[1]

Orabilex[2] and Telepaque[3]

LESLIE A. MORGAN, M.D., and RAYMOND E. PARKS, M.D.

THE SEARCH for the most effective and least toxic medium for oral cholecystographic study began in the 1930's with the introduction of tetraiodophenolphthalein, a relatively harsh and inefficient agent. In the next decade, iodoalphionic acid made its appearance and was generally considered to be a substantial improvement, despite the continued, though lessened, incidence of intestinal and urinary side-reactions. The quest for an oral medium with more favorable systemic acceptance was heightened with the synthesis in 1951 of Telepaque (iopanoic acid), the first of a series of tri-iodinated organic compounds evolved to increase the opacifying power of the ingested agent.

Since the report of Shapiro (1), dissatisfaction with Telepaque has been expressed by several investigators, including Root and Lewis (2). Intestinal concentration of this agent results in frequent superimposition of areas of opacification in the right colon on the gallbladder. Other specific objections were the density of the opacified gallbladder, sufficient on occasion to block out all intravesicular detail, and an annoying persistence of side-reactions in the intestinal and urinary tracts. These difficulties were sufficient to stimulate continued investigation of new media. An important development in this field is Orabilex (Bunamiodyl), subject of an increasing number of highly favorable surveys.

An interesting by-product of this series of creative pharmacology has been the establishment of a comprehensive set of criteria to define the optimal cholecystographic agent. These standards, enumerated by Shehadi (3), were broadened by Shapiro (1) to include the following: (*a*) low toxicity and minimal side reactions; (*b*) prompt elimination; (*c*) selective concentration of the agent in the gallbladder; (*d*) preferential renal excretion to minimize confusing intestinal shadows; (*e*) rendition of an optimal degree of opacification of the gallbladder, insuring maximal diagnostic accuracy, without obscuring significant details within the viscus. Bickham (4) believes that the property of a medium to elicit "maximum opacifying potential of the gallbladder with a single standard dose" should be added to these criteria.

Studies with Orabilex on approximately 1,500 unselected cases referred for biliary evaluation have been reported by Geffen (5), Teplick *et al.* (6), Arcomano *et al.* (7), Tice (8), Bickham (4), and finally Levin *et al.* (9). In each of these instances, however, the study was concerned primarily with evaluation of the medium by appraisal of side-reactions and effectiveness of gallbladder density. Although comparisons with iopanoic acid have been most favorable to Orabilex, it appeared desirable at this time to subject this new medium to the most objective clinical appraisal. For this purpose, we employed as subjects an unselected group of 200 patients referred for biliary tract study. Doses of Orabilex and Telepaque essentially equivalent pharmacologically were distributed to the patients in random manner. These doses were contained in identical capsules and in identical but coded envelopes in a box containing 100 doses each of the two media.

A prescribed interview for each patient to determine the incidence and type of reactions was carried out by one observer

[1] From the Department of Radiology, University of Miami, Miami, Fla. Accepted for publication in May 1959.

[2] E. Fougera Co. 3 (3-butyrylamino-2,4,6-triiodophenyl)-2-ethyl sodium acrylate.

[3] Winthrop Laboratories. 3 (3-amino-2,4,6-triiodophenyl)-2-ethyl propanoic acid.

Upon completion of the study, two radiologists evaluated the roentgen results. This method of approach, the so-called "double-blind technic," is acknowledged to reduce the subjective factor to the lowest level possible.

It was the primary purpose of this study to evaluate by a purely objective method (*a*) the side reactions and adverse effects of the two agents; (*b*) the degree of opacification of the gallbladder and bile ducts; (*c*) the form and amount of residual material within the gastrointestinal tract.

METHOD AND MATERIALS

Orabilex is a slightly soluble sodium salt of a triiodinated organic compound and is eliminated in large amounts through the kidney. It contains 57 per cent iodine by weight in comparison with Telepaque, which contains 67 per cent iodine and is insoluble in water. One hundred doses of Orabilex (6 capsules of 0.75 gm. each) and 100 doses of Telepaque (6 tablets of 0.5 gm. each) were prepared. The Telepaque tablets were pulverized and placed in capsules, identical in color and size with the Orabilex capsules, so that the patient and the radiologist would be unable at the time of the interview to reveal the type of contrast material which had been used. The capsules were placed in small envelopes and sealed. The envelopes were then numbered by the following method. In a random manner, numbers between 1 and 200 were drawn from a box and assigned to each material, a record being kept of each number and the cholecystographic agent it represented. The code sheet was then sealed in a safe place, where it remained until all final results had been recorded.

The envelopes were distributed as the patient was scheduled for examination. The number on the package was recorded, with the patient's name, on a case report interview sheet, which was given to the interviewer the morning of the examination. The interview sheet contained standard questions regarding nausea, vomiting, diarrhea, cramps, allergy, etc., so that the interview for reaction rate might be standardized as well as possible. The patient was instructed to take the six capsules fourteen hours prior to examination time, with no special preparation such as a laxative or enema. The capsules were taken following a fat-free light meal, and food and liquids were withheld thereafter until the examination.

The same dose of each cholecystographic agent was given without respect to the age, weight, or sex of the individual. All patients were adults, either outpatients or inpatients of the hospital. On the morning of the radiographic examination, all were interviewed by the same person, and a record was made on the interview sheet as described. Following routine cholecystographic filming, a fatty meal was given to 67 patients who had received Orabilex and 58 patients who had received Telepaque. Additional films were made fifteen minutes after the meal. In the Orabilex group, ducts were visualized in 38 patients and in the Telepaque group in 36 (see Table II). All of the cholecystographic films were reviewed by two observers. Each case was evaluated as to the degree of opacification, the presence of calculi, duct visualization, and residual contrast material in the gastrointestinal tract. After all these findings had been recorded, the code was consulted and each case record labeled as to the contrast material represented.

FINDINGS

Thirteen patients failed, for various reasons, to return for the radiographic examination and were not included in the study. Of the remaining 187 patients, 92 received Orabilex and 95 received Telepaque, with the results shown in Table I.

Side Reactions: Tolerance for Orabilex was better than for Telepaque, with approximately 50 per cent fewer side-reactions. There was a total of 63 various complaints in the 92 Orabilex cases, as compared with 122 complaints in the 95 Telepaque cases. All of the side reactions

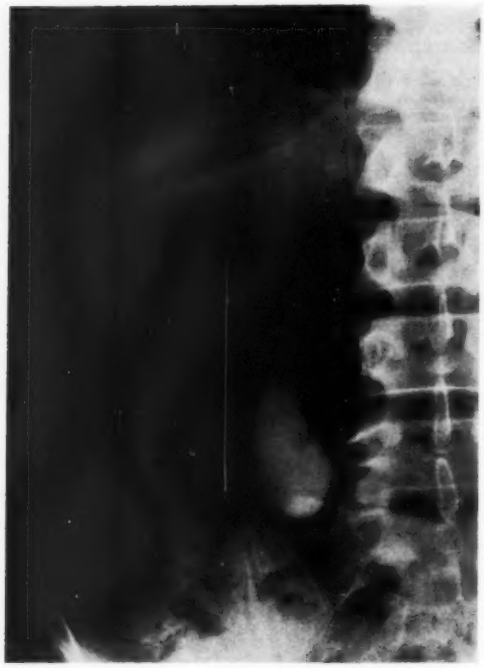

Fig. 1. Normal gallbladder as demonstrated by Orabilex. Note absence of residual medium.

TABLE I: SIDE-EFFECTS OF ORABILEX AND TELEPAQUE

	Orabilex 92 Cases	Telepaque 95 Cases
Nausea		
Slight	12	5
Definite	8	23
Vomiting		
Once	1	1
Repeated	2	1
Cramps		
Vague	10	5
Mild	8	16
Moderate	2	6
Severe	0	3
Diarrhea		
Mild	8	29
Moderate	2	9
Severe		
Dysuria	1	8
Pruritus	2	5
Miscellaneous	9	11
TOTAL COMPLAINTS	65	122*

* Many patients exhibited more than one side-effect.

were delayed in onset beyond thirty minutes to one hour, except in 2 patients who, on further questioning, were somewhat uncertain as to the exact time. As is noted in Table I, the degree of nausea

Fig. 2. Post-fatty-meal film of normal gallbladder obtained with Orabilex.

was somewhat less with Orabilex. One patient receiving Telepaque required emergency treatment for severe nausea, vomiting, and cramps. In no case in which Orabilex was used were the cramps severe, usually being only mild or vague. Diarrhea was approximately four times as frequent in the patients receiving Telepaque. This is possibly due to the modified route of elimination of Orabilex through the kidney. Significantly, however, only 1 patient complained of any degree of dysuria from Orabilex in comparison with 8 cases of dysuria reported with Telepaque. There were 2 cases of allergy in the Orabilex series in comparison with 5 in patients who had been given Telepaque.

All of the examinations in this series were requested and performed for suspected biliary tract disease. Undoubtedly many of the side-reactions were complicated by the patient's prior health, but no attempt was made to exclude any complaint which was mentioned.

Density: The degree of density (Table II) is essentially the same in both series. The number of poor and nonvisualizing gallbladders is the same for both contrast agents. Similarly, in grouping the gallbladders of fair and good visualization,

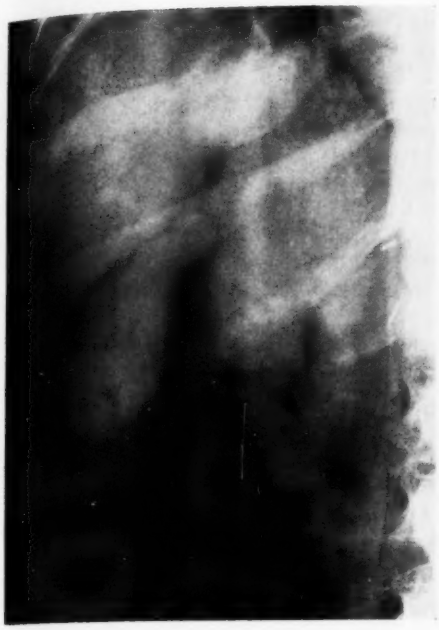

Fig. 3. Numerous small radiolucent calculi demonstrated by Orabilex.

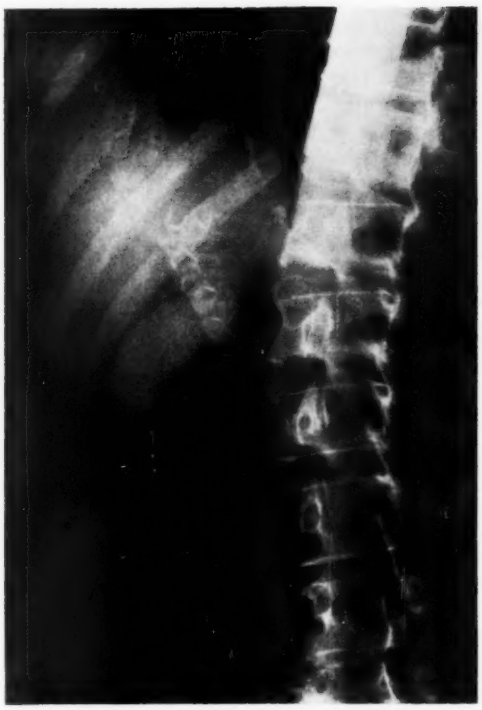

Fig. 4. Multiple calculi, mixed type, present in gallbladder and ducts. Total of twenty-four confirmed upon surgery.

TABLE II: TECHNICAL CRITERIA: ORABILEX AND TELEPAQUE

	Orabilex 92 Cases	Telepaque 95 Cases
Quality of opacification		
Excellent to good	55	47
Fair	9	20
Poor	9	6
None	19	22
Unabsorbed colonic residual		
None	50	28
Trace	39	40
Moderate to dense	3	27
Duct visualization following fat meal	38 of 67	36 of 58

no marked difference was noted, although there was a slightly higher incidence of good opacifications with Orabilex.

As an interesting sidelight, our statistics indicated that the series included 10 patients weighing 200 lb. or more. By chance, 5 had received Orabilex and 5 Telepaque. There was no visualization in the 5 patients who had received Telepaque whereas satisfactory cholecystograms were obtained in 3 of the 5 who were given Orabilex. In some measure this corroborates the postulation that a single dose of 4.5 gm. (6 capsules) of Orabilex may be employed regardless of patient weight.

The degree of opacification of the ducts and the number of patients in whom opacification occurred were statistically comparable. Satisfactory ductal visualization was achieved only after the fatty meal, with both contrast materials.

Residual: In 89 of the patients receiving Orabilex, or 96 per cent, there was either no residual or only a trace to minimal amount. The residual opacity within the bowel was more diffuse; in only 3 cases was it considered to be present in such an amount as possibly to interfere with interpretation of the cholecystogram. The residual medium, if any, was usually in the cecum and ascending colon when large amounts of fecal material were encountered. In no case was the combination of colon staining and fecal material of such density as to be confused with

calculi. In 28 per cent of the Telepaque cases, residual contrast medium was observed in the bowel segment. Its density and discrete character could have posed difficulties in interpretation had the segment been superimposed over the gallbladder.

COMMENTS AND DISCUSSION

The patient tolerance for Orabilex in this series was considerably higher than for Telepaque. As mentioned, there were approximately 50 per cent fewer overall side-reactions with Orabilex than with Telepaque. Definite nausea occurred three times more frequently with Telepaque than with Orabilex, intestinal cramps were generally more marked on all levels, from mild to severe, and diarrhea was notably more conspicuous in those patients receiving Telepaque.

These findings are generally in accord with those of Levin *et al.* (9), reporting on a series of 575 cases studied with Orabilex. These investigators found that, although mild nausea and some vomiting was more frequent with Orabilex, diarrhea was greatly decreased as compared with Telepaque. Tice (8), except for a moderate incidence of nausea, reported a relatively small number of side-effects.

Dysuria is in all likelihood the most important subjective indication of toxicity. Whereas nausea and vomiting and diarrhea are very often attributable to preliminary preparation and pre-existing irritation, as well as to the medium employed, dysuria is more likely due to the route of elimination of the medium. The effectiveness of butyrylation of the amine group in minimizing irritation of the urinary tract has been frequently emphasized (Geffen, 5; Arcomano, 7; and Bickham, 4). Bickham likewise pointed out that iophenoxic acid was originally introduced because, like Orabilex, it is excreted mainly *via* the urinary tract and thereby lessens intestinal residual. Iophenoxic acid, however, causes a substantial degree of urinary discomfort during its passage, obviated in Orabilex by virtue of the principle of butyrylation.

The problem of colonic shadows, frequently encountered with Telepaque, appears resolved with the use of Orabilex. In the great majority of instances, only a trace of the opaque material is present in the colon. Confusing overlapping shadows are virtually eliminated.

CONCLUSION AND SUMMARY

A search for a better tolerated contrast agent for study of the biliary tract than has been available, with as good, or better, visualization and less residual contrast material, led to a "double-blind" comparison of Orabilex and Telepaque. Orabilex was found to have the advantages of better patient tolerance, with far less irritation of the gastrointestinal tract; it provided a high degree of diagnostic opacification, with minimal residual colonic opacification (see Figs. 1–4).

In general, Orabilex better fulfills all of the exacting criteria set forth by Shehadi, Shapiro, and Bickham. We are therefore of the opinion that Orabilex represents the most significant refinement in oral cholecystographic media to date.

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SUMMARIO IN INTERLINGUA

Un Studio Bisocculte de Oral Medios de Contrasto Usate in Cholecystographia: Orabilex e Telepaque

Le desirabilitate de un agente de contrasto pro studios del vias biliari, melio tolerate que le agentes previemente disponibile e resultante in le mesme o un meliorate qualitate de visualisation e in un plus leve residuo, ha suggerite le presente studio comparative de Orabilex e Telepaque. Un "bisocculte" studio clinic pro evalutar le meritos del duo medios esseva effectuate in 187 patientes presentate al examine.

Esseva constatate que inter le duo medios, Orabilex esseva melio tolerate, causava minus irritation del vias gastrointestinal, e produceva un alte grado de visualisation, con un minimo de residue opacification colonic.

Es opinate que iste nove medio representa le plus significative raffinamento in cholecystographia oral usque a iste tempore. Illo es un levemente solubile sal natrial de un tri-iodate composito organic e ha le formula acrylato de natrium 3(3-butyrylamino-2,4,6-tri-iodophenyl)-2-ethylic. Illo es eliminate primarimente via le renes.

Gastric Carcinoma: Accuracy of Radiologic Diagnosis[1]

N. M. STRANDJORD, M.D.[2] R. D. MOSELEY, JR., M.D.,[3] and R. L. SCHWEINEFUS, M.D.[4]

SEVERAL RECENT publications, notably those of Yerushalmy (1) and Garland (2), have been concerned with the accuracy of interpretation of diagnostic procedures. While particular emphasis was placed on the analysis of the radiologic examination of the chest, attention was also called to other types of diagnostic examination, such as the electrocardiogram. Garland (2), investigating error in the interpretation of serial chest films, found about 30 per cent disagreement between two physicians, while a single interpreter was likely to disagree with himself 20 per cent of the time.

The radiologic examination of the upper gastrointestinal tract depends, in addition to the interpretation of the films, upon a fluoroscopic impression. The accuracy of this method as it relates to the problem of gastric cancer was discussed by Klayman *et al.* (3). In his series of 75 cases, 22 were reported as "nonmalignant" and 9 were called indeterminate on x-ray study. The failure rate for exfoliative cytology was 15 out of 75, or 20 per cent.

Our interest in the problem has been further stimulated by the article by Raskin *et al.* (4) reporting a failure of 5 per cent for exfoliative cytologic technics. In 19 per cent of these patients the x-ray diagnosis was "no cancer." The figures do not include 4 false positive cytologic diagnoses in 740 patients who were normal or had benign conditions. To answer some of the questions raised by these figures, we have undertaken a review of the radiologic diagnosis of gastric cancer observed at The University of Chicago Clinics from January 1950 through December 1957. This is the period covered by both of the above reports of cytologic examinations.

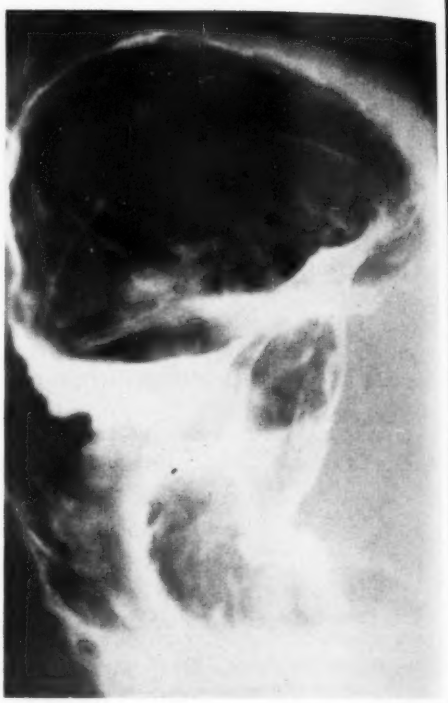

Fig. 1. Incorrect interpretation: J. K., 67-year-old male.
The fluoroscopist described a lesion of the body of the stomach but felt that the films did not support this impression and concluded "normal stomach." Cytology positive for cancer.

During this period, approximately 32,000 individual examinations of the upper gastrointestinal tract were performed. These were conducted by thirty-five different examiners in various phases of residency training and staff positions. All patients were examined fluoroscopically, with modifications of the technic described by Templeton (5). In all cases films made on the filming fluoroscope, demonstrating

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[3] Professor and Chairman, Department of Radiology, The University of Chicago.
[4] Lt. (MC) U.S.N., U. S. Naval Hospital, Oakland, Calif.

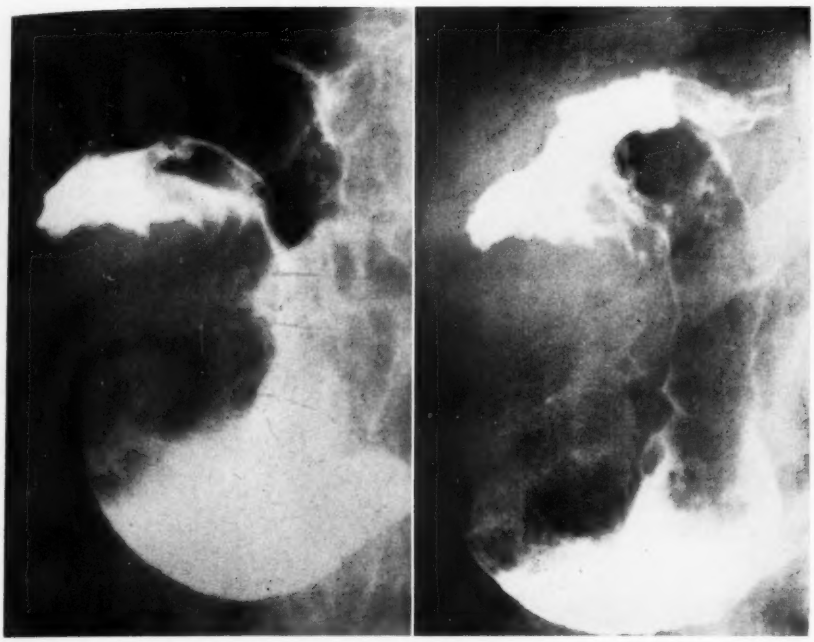

Fig. 2. Incorrect interpretation: J. B., 68-year-old male.
The clinical information was "enlarged spleen." Radiologic interpretation was large spleen impressing the stomach. Cytology positive for cancer.

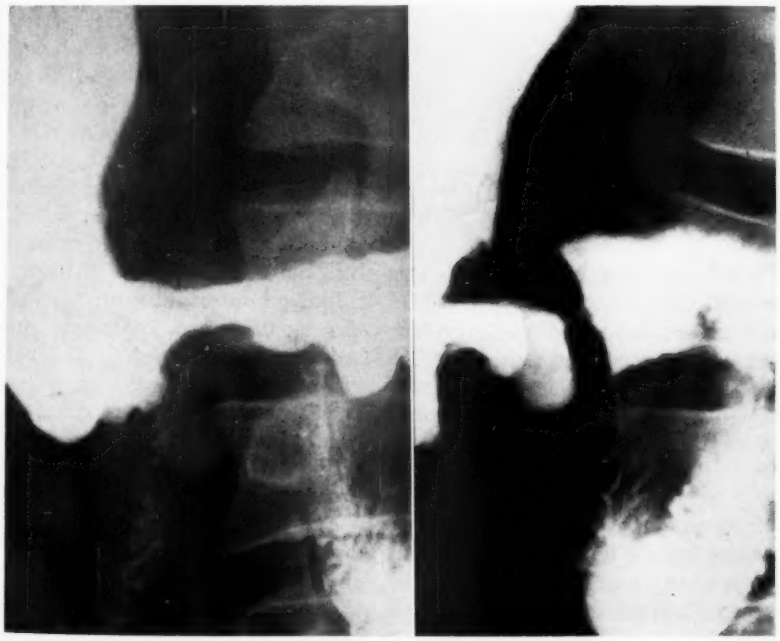

Fig. 3. Incorrect interpretation: N. M., 38-year-old male.
Clinical information, "pancreatic cyst." Lesion noted and interpreted as "extrinsic pressure by a pancreatic cyst." Cytology negative for cancer.

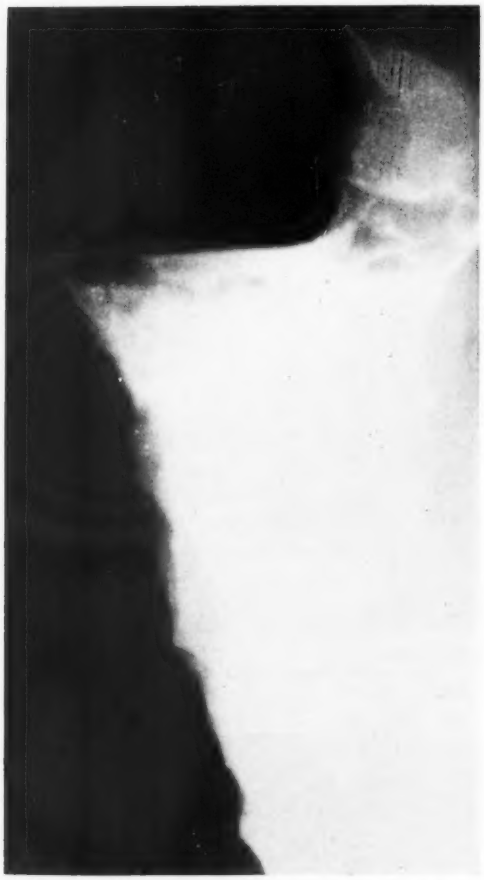

Fig. 4. Fundal lesion: V. S., 72-year-old male. Fluoroscopically a lesion was described in the fundus. Films interpreted as normal. Lesion is demonstrated in retrospect.

mucosal relief and profile views of the filled stomach and duodenum, were obtained. During this period, 371 gastric cancers were diagnosed and are recorded in our Registry of Neoplastic Diseases.

Eighty-eight of these 371 cases are not included in this analysis because the primary radiologic examinations were not done in our department. These patients either underwent surgery for gastric cancer at another institution and were seen in our clinic with recurrence or were not referred to the Department of Radiology prior to surgery or autopsy. The remaining 283 cases were analyzed completely.

We believe that in the vast majority of instances the radiologic diagnostic impression should be unequivocally normal or abnormal; and, if abnormal, an attempt should be made to reach a definitive pathological diagnosis, if possible, by this technic. It is to be remembered that in a small number of cases it is impossible to differentiate between inflammatory disease and malignant disease of the antrum, especially if complete obstruction is present, or between benign and malignant ulcers.

We have analyzed the 283 cases, using the following criteria.

Correct Diagnosis: An outright diagnosis of cancer or, in some cases, cancer as a strong first in a differential diagnosis.

Cannot Differentiate: Lesion found and described, but differentiation between benign and malignant could not be made.

Incorrect or Failure: Lesion called normal or benign or misinterpreted, for example, as a cyst of the pancreas or a large spleen.

In all cases, the x-ray films, cytologic, gastroscopic, and operative reports, surgical pathologic data, and autopsy records have been analyzed. With the above criteria, the correct diagnosis was made radiologically in 219, or 78 per cent, while in 18, or 6 per cent, a differentiation was not possible. The failure rate is 16 per cent. It should be noted, however, that in only 14 of the 46 cases interpreted by these criteria as failures was the radiologic interpretation "normal." Thus, the accuracy of radiologic detection of lesions in this series of 283 patients was 95 per cent. The higher level of inaccuracy was in the differentiation of lesions and interpretation of the findings rather than in the recognition of a deviation from normal.

Cytology was performed in 157 of the 283 cases, for the most part with the chymotrypsin lavage technic (3, 4). In this series 24 patients, or 15.3 per cent, were incorrectly called normal. There were 13 failures in 67 cases seen in 1950–1954,

or 19 per cent, and 11 failures in 90 cases seen between 1955 and 1957, 12 per cent.

Of the 75 cases reported by Klayman *et al.* (3), we have eliminated 12 in which previous gastric resection had been done for carcinoma, leaving 63 cases for analysis. Four additional cases of gastric carcinoma were found in which the cytology was negative, giving 13 failures out of 67 cases, a 19 per cent failure of cytology. If one adds these 4 failures to Klayman's published report, the figure would be 19 out of 79, or 24 per cent failure. In 90 cases in the present series seen from 1955 through 1957, there were 11 failures of cytology, or 12 per cent. The difference between Raskin's figure of 5 per cent and our 12 per cent is explained by the fact that some patients previously considered to have been benign by exfoliative cytology have subsequently succumbed to or have been demonstrated to have cancer of the stomach. There is no statistically significant difference in the failure rate for these two time periods. It should also be pointed out that in the majority of these cases cytology was done on patients in whom a roentgen diagnosis of gastric neoplasm had been previously made.

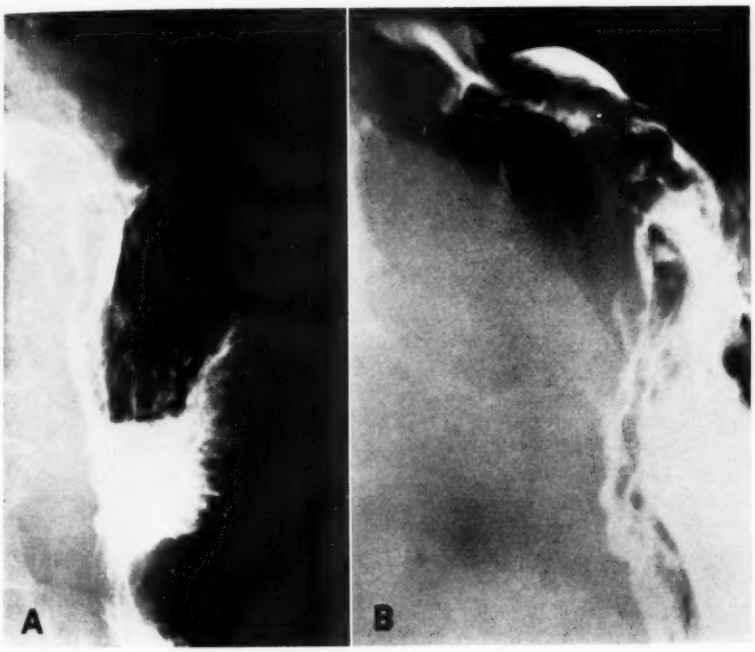

Fig. 5. Fundal lesion. J. W., 83-year-old male.
A. Examination Aug. 9, 1955, interpreted as normal.
B. Examination two years later, Sept. 25, 1957, leading to diagnosis of carcinoma. In retrospect, the lesion was present in 1955. Cytology positive for cancer.

We are naturally interested in this comparison of the accuracy of radiologic examination and cytologic technic but are actually more concerned with our failures and what can be done to improve the radiologic diagnosis. The problem can be approached in several ways.

LOCATION OF THE LESION

Does the location of the lesion affect the accuracy of x-ray diagnosis? It will be noted that the percentage of error in any location is not greatly different from the actual percentage of lesions in that location (Table I). This does not mean,

however, that the location is irrelevant to the accuracy of radiologic diagnosis. In the case of disease of the fundus, 7 of the 8 lesions are clearly demonstrated on the films but were missed at the time of original interpretation. The most significant factor in failure of diagnosis in the body of the stomach site is the inability to distinguish maligant from benign ulcers. In the antrum we are so cognizant of our inability to differentiate gastritis from neoplasm that the percentage of frank failure in this area is reduced, since the x-ray diagnosis frequently is inconclusive.

Of the 18 cases in which the radiologist would not make a differentiation between malignant and benign disease, 7 were ulcers without a mass; 10 were antral lesions with or without obstruction; 1 was listed as either giant rugal gastritis of the antrum or neoplasm. We do not consider these errors but a recognition of the frequent inability to distinguish between lesions of these types.

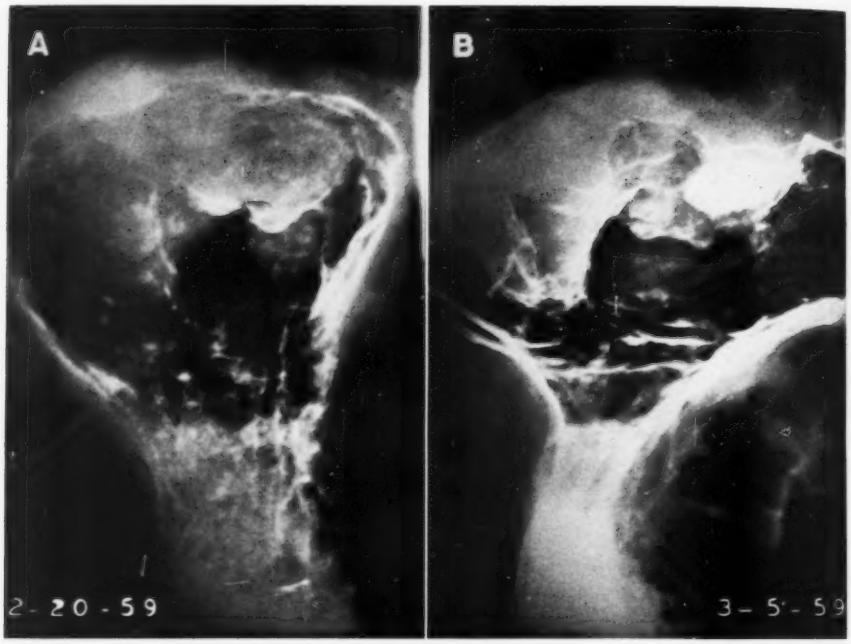

Fig. 6. Fundal lesion: A. K., 60-year-old male.
A. Large mass in fundus interpreted radiologically as "malignant neoplasm." Cytologic examination negative three times. Gastroscopic interpretation, giant rugal gastritis three times. Direct biopsy through gastroscope showed normal gastric mucosa on two occasions and normal esophagus twice.
B. Re-examination, with distention by CO_2, again interpreted as demonstrating malignant neoplasm. Surgery confirmed the radiological diagnosis.

TABLE I: POSITION OF LESION IN 283 CASES

	Cases	Failures
Fundus	51 (18%)	8 (18%)
Body	102 (35%)	22 (47%)
Antrum	107 (38%)	11 (24%)
Linitis plastica	23 (8%)	5 (11%)
	283 (100%)	46 (100%)

RADIOLOGIC FAILURES

The 46 failures are more interesting: 32 patients were noted to have lesions but these were misinterpreted as benign; 14 cases were called normal. In 7 of the latter group the films in retrospect are normal. Two of these cases at autopsy showed a tiny scar in the stomach, which on section revealed carcinoma; there were widespread metastases. These cases em-

phasize the fact that the size of a gastric tumor is not necessarily related to prognosis. In the remaining 7 cases called normal, the lesions were obvious on retrospective examination of the films. Figure 1 demonstrates such a lesion.

There is no question that the best care of the patient is assured when the radiologist is cognizant of the pertinent clinical findings. However, Figures 2 and 3 illustrate the great necessity of approaching the interpretation of the radiologic findings with a high degree of objectivity, regardless of the subjective impression formed on the basis of history and physical examination.

Fundal lesions presented a special problem. Of 51 cases, 8 were not correctly diagnosed. In 7 of these, the lesion is well demonstrated. Figures 4 and 5 illustrate typical fundal lesions which were overlooked and are easily seen in retrospect. A recent case (Fig. 6) demonstrates that the radiologist must stand firm and interpret unequivocal findings, irrespective of negative gastroscopy and cytology.

ULCERS WITHOUT MASS

The number of patients with ulcers and no associated mass was small, totaling 27. Fourteen cases were interpreted as showing definite criteria of malignancy and were considered outright cancer or most probably cancer. In 7 cases the radiologist would not differentiate. Five cases were interpreted as benign and 1 was missed entirely.

Figures 7–10 represent typical examples of the difficulties encountered in the diagnosis of malignant gastric ulcers. Figures 11 and 12 illustrate radiological

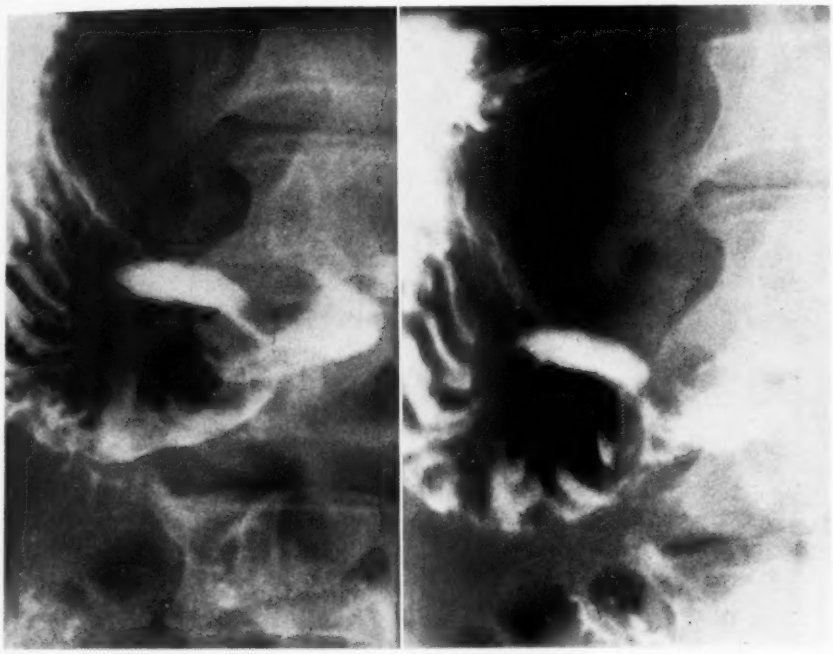

Fig. 7. Gastric ulcer called benign: P. L., 71-year-old male.
Interpreted as "huge benign ulcer, lesser curvature." Pre- and postoperative diagnosis benign. Sections demonstrated carcinoma.

TABLE II: FAILURE OF CYTOLOGY IN DIAGNOSIS

X-ray Diagnosis	No. of Cases	Failure by Cytology
Cancer	219	9/109 (8%)
Inconclusive	18	4/12 (33%)
Normal or benign	46	10/35 (38%)

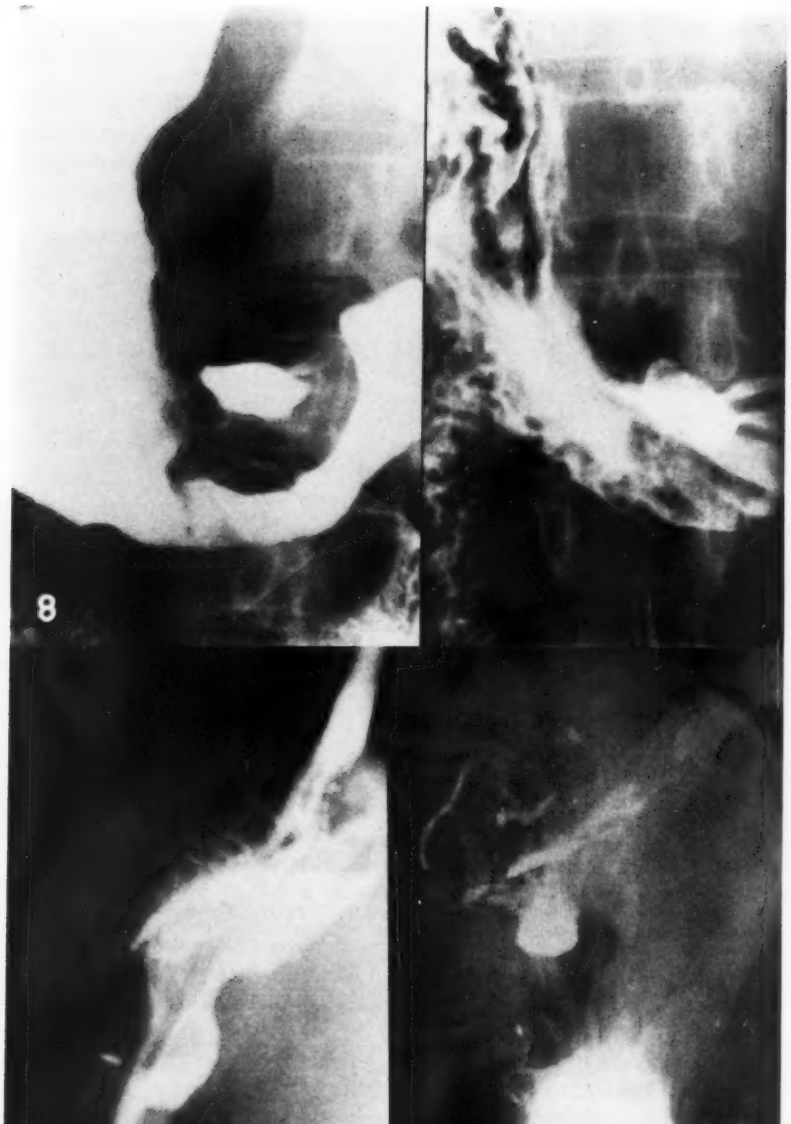

Fig. 8. Gastric ulcer, indeterminate: F. P., 53-year-old female.
Interpreted as either benign or malignant by x-ray. Cytology negative. Pre- and postoperative diagnosis benign. Surgical pathology demonstrated carcinoma.
Fig. 9. Gastric ulcer, indeterminate, F. D., 46-year-old male.
Radiological diagnosis, "benign? malignant?" Gastroscopy described benign lesion. Cytology benign. Pre- and postoperative diagnosis benign. Surgical pathologic diagnosis malignant.

healing of malignant gastric ulcers under medical management. In the case illustrated in Figure 11 the ulcer was not present in the surgical specimen.

PREOPERATIVE AND POSTOPERATIVE DIAGNOSIS

Of the 64 cases diagnosed by the radiologist as normal, benign, or inconclusive, 7 did not come to operation here. In the remaining 57 a combination of x-ray examination, gastroscopy, cytology, and other laboratory data supported a preoperative diagnosis of cancer in 40; 17 cases had a preoperative diagnosis of benign gastric lesion. Of these 17, 8 were called malignant by the surgeon. In 9 cases it remained for the surgical pathologist to make the correct diagnosis.

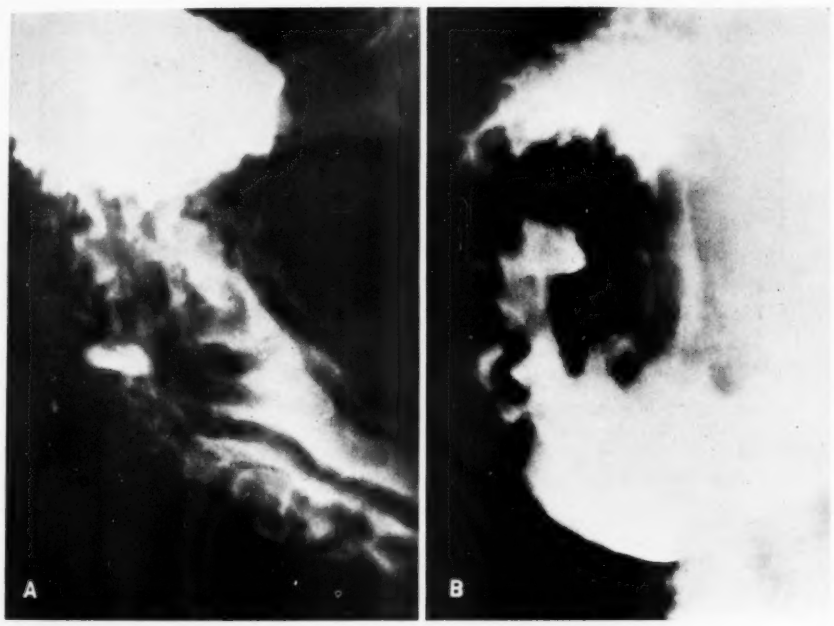

Fig. 10. Gastric ulcer: S. S., 38-year-old male.
A. The first examination, on Feb. 27, 1952, was interpreted as normal. The gastroscopist saw a lesion and interpreted it as benign. Review of the films demonstrated this lesion on one frame. Cytology negative on two occasions.
B. Lesion, missed initially, examined again, June 20, 1952, had increased in size and was considered malignant. Preoperative diagnosis benign. Postoperative diagnosis malignant.

DISCUSSION

It is apparent that the most important conclusion that we should draw from this investigation is just how accurate we can be, as physicians, in the diagnosis of gastric neoplasm, utilizing all the facilities at the command of modern medicine—x-rays, gastroscopy, exfoliative cytology, and chemical and laboratory studies.

By utilization of all technics, a diagnosis can be made preoperatively in 94 per cent. There can be no question that x-ray diagnosis holds now and will continue to hold a pre-eminent place in the diagnosis of gastric neoplasm, especially from the standpoint of detection of the lesion and, in most cases, its differentiation.

Cytology appears to have its highest accuracy in the same group of cases in which x-ray diagnosis was definitive. If the radiologist misdiagnosed normal or benign or could not differentiate, the inaccuracy of the exfoliative cytologist becomes 33 to 38 per cent (Table II).

Gastroscopic results are difficult to evaluate, as many failures are classified

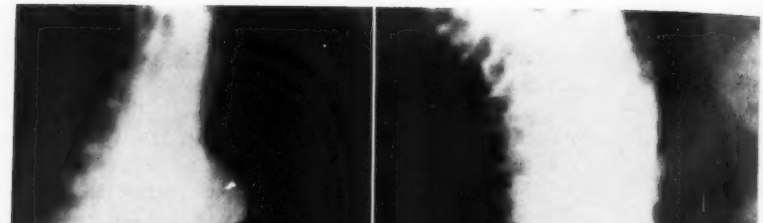

Fig. 11. Malignant gastric ulcer, healing: R. W., 58-year-old female.
A. The lesion was called a benign ulcer on Nov. 23, 1954.
B. Re-examination, Jan. 25, 1955, failed to demonstrate the ulcer. Cytology now positive for malignant cells.

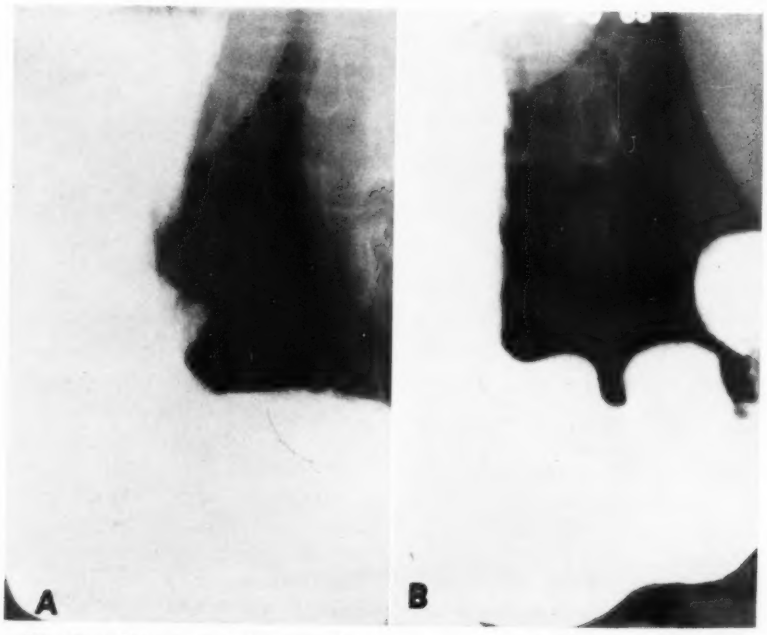

Fig. 12. Malignant gastric ulcer with apparent healing: A. G., 67-year-old female.
A. On March 1, 1957, the radiologic interpretation was "Appearance speaks in favor of malignancy." Cytology negative for cancer.
B. Re-examination April 20, 1957, interpreted as showing normal stomach. Patient died subsequently of gastric cancer.

as unsatisfactory examinations. In our 64 cases without a positive diagnosis of carcinoma by x-ray, the positive diagnosis by gastroscopy was 38 per cent.

CONCLUSIONS

1. Radiologic examination of the stomach has an unchallenged place in the detection of deviations from normal. In this series, some abnormality was found in 95 per cent of the cases.

2. Human error, which it is hoped can be diminished by increased attention and experience, contributed to the failure rate. However, the radiologist must keep continually in mind the difficulty in differentiating antral lesions, some gastric ulcers, and his inability to detect lesions of microscopic size.

3. Cytologic technics should not be considered competitive but, rather, should be viewed as contributing to the extension of accuracy in differentiation and diagnosis. In this series it would appear that the radiologist, the cytologist, and the surgeon had their greatest difficulty with the same groups of patients.

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SUMMARIO IN INTERLINGUA

Carcinoma Gastric: Accuratia del Diagnose Radiologic

Esseva analysate 283 casos de cancere gastric con le objectivo de determinar le accuratia del diagnose radiologic. Le correcte diagnose esseva facite radiologicamente in 219 casos, i.e. in 78 pro cento del serie total. In 18 casos, i.e. 6 pro cento, un lesion esseva constatate e describite, sed le differentiation inter benigne e maligne non esseva possibile. Le proportion de non-successos—i.e. de casos judicate como normal o misinterpretate como benigne o como un altere lesion, per exemplo como cyste pancreatic—esseva 16 pro cento. Tamen, inter le 46 casos que esseva assi diagnosticate erroneemente, solmente 14 esseva misdesignate como normal. Per consequente, le accuratia in le detection de un lesion amontava a 95 pro cento.

Studios cytologic esseva effectuate in 157 casos, e super iste base 15,3 pro cento esseva designate como normal. Il pare que iste methodo es le plus accurate in le mesme gruppo de casos in que etiam le diagnose per radios X esseva definitive.

Sin dubita, le diagnose per radios X ha currentemente e va continuar haber un function pre-eminente in le diagnose de neoplasmas gastric, specialmente ab le puncto de vista del detection, sed in le majoritate del casos etiam ab le puncto de vista del differentiation inter malignitate e ulceres benigne.

Pyloric Antral Mucosal Diaphragm with Transpyloric Mucosal Prolapse[1]

ABRAHAM MELAMED, M.D., ROBERT S. HAUKOHL, M.D., and ROBERT E. CALLAN, M.D.

FIVE CASES OF pyloric antral mucosal diaphragm are reported in the literature (1–5). To these we wish to add a case which was complicated by transpyloric gastric mucosal prolapse. The diaphragm, we believe, prevented the normal cephalad movement of the gastric mucosa during peristalsis (Golden's phenomenon). It therefore remained "trapped" in the antrum and its prolapse into the duodenum was easily demonstrated.

CASE REPORT

A 62-year-old white male consulted his physician (R. E. C.) on Sept. 14, 1957, two days after the sudden development of severe pain in the right upper quadrant of the abdomen. This was accompanied, twelve hours after the onset, by the passage of approximately one ounce of bright red blood per rectum. The pain radiated to the back and was not influenced by eating. There was no history of nausea, vomiting, or weight loss. Physical examination showed spider nevi over the anterior chest wall, enlargement of the liver 4 cm. below the costal margin, a reducible right inguinal hernia, and a slightly enlarged smooth right lateral prostatic lobe. Proctoscopic examination revealed internal hemorrhoids without evidence of recent bleeding. No evidence of organic disease was obtained by barium enema studies. Pertinent laboratory findings were occult blood in the stool (4+), absence of free HCl, and presence of lactic acid in the gastric contents.

Barium meal studies on Nov. 5, 1957, revealed no abnormality in the esophagus, but a constant zone of narrowing was encountered in the distal stomach 2.5 cm. proximal to the base of the duodenal bulb (Fig. 1). The narrowed segment measured 2 to 3 mm. in length, and the luminal diameter was approximately 8 mm. No rugal pattern was recognizable adjacent and cephalad to the diaphragm. Thickened rugae, however, were discernible in the "compartment" between the collar-like narrowing and the pyloric canal, prolapsing into the duodenum during antral systole (Fig. 1). During the prolapsing phase the "compartment" was considerably shortened (approximately 10 to 15 mm.). The duodenum was otherwise essentially normal. The diagnosis was "a diaphragm-like structure in the pyloric antrum with transpyloric mucosal prolapse."

Surgical exploration by Dr. Guzzetta at Misericordia Hospital (Milwaukee) on Nov. 20, 1957, revealed an area of thickening in the antrum of the stomach. Gastrotomy disclosed a hymen-like membrane in the distal antrum, and resection of the distal half of the stomach was performed. Following operation upper abdominal complaints ceased except for one episode of upper abdominal fullness in December 1957.

The patient is now suffering from inoperable (fibro?) sarcoma involving the right chest and is expected to succumb to this disease. Exploratory thoracotomy was done at Milwaukee County General Hospital, Wauwatosa, Wisc.

Pathological Examination: The operative specimen consisted of the distal portion of the stomach, including the pyloric sphincter and a short length of proximal duodenum. The stomach measured approximately 15 cm. along the lesser curvature in the fresh state. The serosa was smooth and intact. At the distal end was a redundant circumferential fold of gastric mucosa which on the slightest pressure could be forced to protrude through the pyloric sphincter into the lumen of the proximal duodenum (Fig. 2). The pyloric orifice was of normal caliber. Proximal to the pylorus, at a point about 3 cm. from the sphincter, there was a demonstrable membrane of gastric mucosa that divided the distal stomach into two chambers. A small slit-like aperture about 1.0 cm. in maximum diameter was demonstrated in this membrane near its attachment to the lesser curvature on the posterior wall. The membrane was readily movable in either direction. It was best viewed from the proximal surface (Figs. 3 and 4). The gastric mucosa, throughout, was intact.

The specimen was distended with cotton and fixed without opening. After complete fixation, a coronal section displayed the membrane to much better advantage (Fig. 5). Again no defect of gastric mucosa could be demonstrated. The muscular layer of the stomach wall did not extend into the mucosal fold, and its continuity was maintained at the base of the fold. Whole-organ histologic preparations (Fig. 6) showed the membrane mentioned above to consist of intact gastric mucosa, the muscularis mucosae, and the submucosa. The muscularis of the stomach wall did not participate in the membrane formation. There appeared to be moderate hypertrophy of the muscle in the prepyloric portion of the stomach; the muscle in the proximal portion was of normal thickness.

[1] From the Departments of Radiology and Clinical Pathology, Evangelical Deaconess Hospital; Department of Pathology, Marquette University Medical School; Departments of Pathology and Surgery, Misericordia Hospital, Milwaukee, Wisc. Accepted for publication in May 1959.

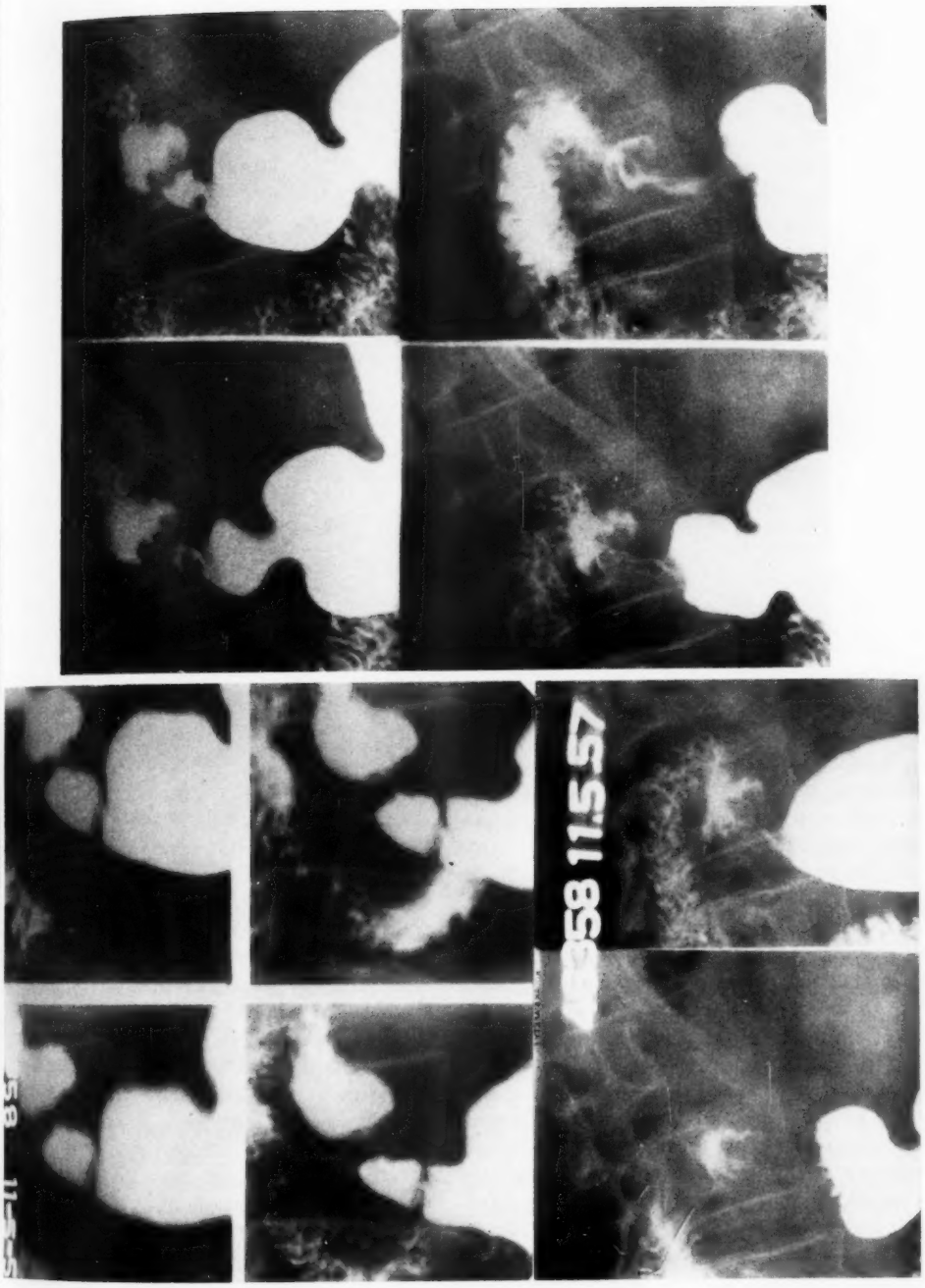

Fig. 1. Serial x-ray views showing diaphragm in antral portion of stomach and prolapse of "prepyloric" mucosa into the duodenum. Prolapse is seen when the "compartment" is contracted.

REVIEW OF LITERATURE

Touroff and Sussman (1) in 1940 claimed that their case of congenital prepyloric membranous obstruction in a four-week premature infant was the first in the literature. Failure to pass meconium and marked gaseous distention of the stomach were relieved by surgery. Multiple incisions in the prepyloric septum and pyloroplasty were performed.

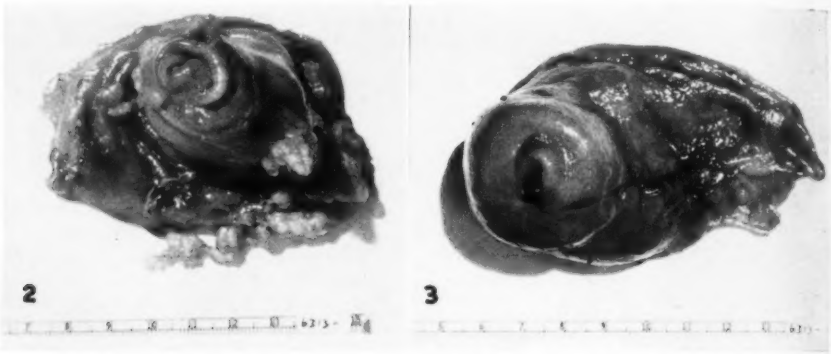

Fig. 2. Distal end of resected stomach showing redundant circumferential fold of prepyloric gastric mucosa protruding through the pyloric ring.
Fig. 3. Proximal view of resected stomach with entire specimen everted. The small vertical split represents the aperture in the gastric membrane.

Sames (2), in 1949, described a prepyloric mucosal diaphragm in a forty-year-old woman who had been treated for an apparently unrelated chronic gastric ulcer. This diaphragm, which measured 3 mm. in thickness and was located 15 mm. proximal to the pyloric canal, contained an eccentric opening measuring 3 to 5 mm. in diameter. Microscopic studies of the specimen showed no evidence of ancient or recent peptic ulcer in this region. Sames believed that the diaphragm represented a congenital anomaly.

In 1953, Gross and Durham (3) reported a hymen-like ring of mucosa, muscularis mucosa and submucosa in a thirty-five-year-old female, who complained of intermittent vomiting of several years duration, aggravated by solid food and partially relieved by a fluid diet. Five abdominal and pelvic operations for these symptoms prior to discovery of the gastric anomaly failed to afford relief. During the sixth operation gastrotomy revealed a thin septum measuring 2 to 3 mm. in thickness. A Finney pyloroplasty, with inclusion of the membrane in the anastomosis, resulted in a cure.

In 1953 Rota (4) attended a 74-year-old female with a history of intermittent attacks of nausea and vomiting followed by diarrhea over a period of eight years. Symptoms occurred in the late evening or early morning and were not related to diet. The patient lost about 21 pounds in eight months. The vomitus consisted of undigested food and no bile. X-ray diagnoses made in 1942 and 1944 were "pyloric obstruction with 25 per cent retention in twenty-four hours" and "thickening of pylorus due to either scirrhous carcinoma or scar tissue of healed ulcer," respectively. The surgical specimen showed a mucosal diaphragm with a 4-mm. central opening. The gastric mucosa immediately cephalad to the diaphragm was reddened, flattened, and finely pebbled. The fundic mucosa was pale and rugose. The microscopic changes consisted primarily of lymphocytic infiltrations. There was no evidence of scarring. A diagnosis of "chronic gastritis of the pyloric antrum" (cephalad to the diaphragm) was made.

Despirito and Guthorn (5), in 1957 reported pyloric obstruction and gastric perforation in a newborn infant in whom a diagnosis of meconium peritonitis was made

Fig. 4. Proximal view of fixed specimen. The prepyloric membrane is demonstrated to have but a narrow slit-like aperture on the lesser curvature side.

Fig. 5. Coronal section of fixed stomach with both halves displayed. The mucosal membrane clearly separates the distal stomach into two chambers. A wooden stick lies within the membrane aperture.

radiographically at twenty-six hours of age. The gastric perforation was overlooked during the first operation, when a temporary jejunostomy was performed. Prepyloric obstruction was later detected by x-ray examination, at three weeks of age. The second operation disclosed a large diaphragm with a 5-mm. opening immediately proximal to the pylorus. As a result of their experience, the authors suggest

Fig. 6. Histologic macrosection of entire specimen cut in a coronal plane. The membrane is composed only of mucosa, muscularis mucosae, and submucosa. The muscularis is not involved.

contrast media studies preoperatively to obviate temporizing jejunostomies.

DISCUSSION

Prepyloric mucosal diaphragm seems to be of exceedingly rare occurrence. The congenital theory of origin is favored by most writers on the subject. Gross and Durham (3) believe that embryologically this lesion is similar to congenital stenosis and atresia of the esophagus and duodenum. They state that at the 7 to 9-mm. stage of the human embryo the esophagus and stomach are solid for a brief period. The membrane probably arises during this stage at a spot where secretion vacuoles fail to develop and produce a lumen. Into the resulting solid mass of cells the submucosa from the sides grows in a ring-like form. The ultimate anomaly, *i.e.*, atresia, stenosis, or a diaphragm, depends upon the size and position of the developmental failure. Others have considered the condition to be acquired, but proof is lacking.

A mucosal diaphragm may cause symptoms immediately after birth or during adult life. It is difficult to understand why patients with this abnormality experience little or no discomfort for many years, sometimes into old age. This "quiescent" period may be one of tolerable or sub-

clinical discomfort. Under the influence of gastritis, edema of the diaphragm and/or narrowing of the foramen, patients experience increased discomfort and then seek medical advice.

Symptoms evidently are dependent on the size and location of the opening in the diaphragm. If the outlet requirements are fulfilled, the size of the foramen is compatible with a normal existence or one in which the patient learns to cope with his deficiency by limiting his food intake, masticating more thoroughly, etc. Stomach contents entering the duodenum are fluid or semifluid. Unless considerable narrowing exists or complications ensue, patients seem to experience little difficulty. It is interesting to note that this anomaly has been described in symptomatic patients only. As far as we can ascertain from the literature, it is not encountered in clinical or autopsy surveys or as an incidental finding.

The physical findings and laboratory data seem to be of little value or significance in uncomplicated cases. The diagnosis can be made by gastrotomy and/or x-ray examination. Smooth luminal narrowing with a diaphragm-like filling defect having a central or eccentric opening is pathognomonic. The x-ray diagnosis can be made if such possibility is considered. The orifice in the diaphragm should vary little, if at all, during the course of x-ray studies, but best visualization is obtained during antral diastole. The chronicity and severity of the narrowing are probably inversely proportional to the prominence or thickness of the rugae immediately cephalad to the diaphragm. Exaggerated peristaltic waves proximally result in effacement of the corresponding rugae. Caudad to the diaphragm, however, there should be a tendency toward the development of transpyloric mucosal prolapse. Cephalad movement of such mucosa during systole—Golden's phenomenon—is prevented by the diaphragm. Our case is an excellent illustration of the pathogenesis of transpyloric mucosal prolapse.

The differential diagnosis of narrowings in the distal stomach is made considerably simpler by serial views of the gastroduodenal junction. The importance and value of these views cannot be overemphasized. There are actually very few, if any, distal gastric narrowings which might simulate a diaphragm. Perhaps the only condition that will produce such a deformity is a cystogastrocolic ligament (6). This is reported as a band or fold of peritoneum which stretches from the fundus or neck of the gallbladder across the duodenum and sometimes the distal stomach to the greater omentum or the transverse colon. When and as it crosses the pyloric antrum, it may cause a marked deformity of that portion of the stomach. This ligament may vary from a thin flat membrane to a thick dense band. The pyloric canal may be flattened and compressed, simulating malignant infiltration or even a diaphragm. A diaphragm will be simulated if the ligament is in the form of a band. There is no interference with peristalsis in the case of a diaphragm, but with the cholegastrocolic ligament peristalsis may be hampered by compression.

Most authors include a circumferential redundant fold of mucosa in the differential diagnosis. Such redundancy is characterized by exaggerated rugal pattern, inconstant position, varying luminal diameter, etc. Variability or inconstancy is the distinguishing feature of this condition, and it is usually accompanied by generalized rugal thickening. Microscopic studies of true diaphragmatic membranes show no characteristics of rugal formation.

Problems involving strictures of the distal stomach due to scarring or neoplastic disease can be resolved by gastric lavage and adequate serial visualization. In the previous reports of gastric diaphragms there was no evidence of peptic ulcer or scarring.

Theoretically, ectopic smooth muscle or pancreatic tissue might produce an appearance somewhat similar to diaphragms but such lesions are usually rounded and eccentric in position, frequently containing ulcer craters.

TREATMENT

Adult patients probably exhaust conservative measures before consulting a physician. As mentioned above, these patients modify their eating habits and diets in an effort to relieve their discomfort. When such measures no longer afford relief, a physician is consulted. X-ray examinations will reveal narrowing in the distal stomach. When the unrelenting nature of the narrowing becomes apparent, surgery is indicated. In the newborn surgical intervention is necessary because of severe obstructive phenoma. Incision of the diaphragm, enlargement of the foramen, or resection of the diaphragm-bearing portion of the stomach has resulted in cure.

SUMMARY

A prepyloric mucosal diaphragm complicated by transpyloric mucosal prolapse is reported in an elderly white male who experienced symptoms late in life. Etiology, symptoms, surgical, pathological, and roentgenological findings in this condition are discussed. The roentgenographic appearance is quite characteristic and distinctive. In any case of prepyloric obstruction or narrowing, the possibility of a prepyloric mucosal diaphragm should be considered. Surgery is necessary to relieve symptoms.

This case report constitutes proof of Golden's phenomenon. The diaphragm prevented normal cephalad movement of the gastric mucosa during antral systole, thereby creating circumstances favorable to the development of prolapse into the duodenum.

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SUMMARIO IN INTERLINGUA

Diaphragma Mucosal Pyloro-Antral con Prolapso Mucosal Transpyloric

Un diaphragma mucosal prepyloric, complicate per prolapso mucosal transpyloric esseva trovate in un masculo de racia blanc de etate avantiate qui habeva experientiate symptomas a un tempore tardive de su vita. Iste anomalia es de un occurrentia extrememente rar; illo es generalmente considerate como de origine congenite. Il pare que le symptomas depende del dimensiones e del loco del diaphragma. Le diagnose pote esser facite per gastrotomia e/o roentgenoscopia. Un restriction lisie del lumine con un diaphragmoide defecto de replenation a apertura centric o eccentric es pathognomonic pro le condition.

Es opinate que le hic reportate caso demonstra le validitate del phenomeno de Golden. Le diaphragma preveniva un normal movimento cephalotrope del mucosa gastric durante le systole antral, creante assi circumstantias favorabile al disveloppamento de un prolapso a in le duodeno.

The Consequences of the Continuous Ingestion of Sr^{90} by Mice[1]

MIRIAM P. FINKEL, Ph.D., PATRICIA J. BERGSTRAND, B.S., and BIRUTE O. BISKIS, M.D.

MAN HAS BEEN eating food contaminated with Sr^{90} for the past fourteen years. The hazard associated with the deposition of this radioelement in the body can be evaluated to some extent through information gained from animals that have been injected with Sr^{90} solutions. The consequences of internal radiation from material obtained through the diet over a long period, however, may be quite different from the consequences of internal radiation from material obtained from a single injection. This was recently seen to be the case when rabbits were fed large amounts of radiostrontium (1). There has been no information up to this time pertaining to the response of laboratory animals to the continuous ingestion of very small amounts of Sr^{90}. This deficiency, coupled with the difficult problems always associated with the transfer of animal data to man, has placed any estimate of the risk involved from the present and expected contamination of the biosphere in the realm of almost pure conjecture.

A fundamental difference between administering radiostrontium in a single injection or feeding it continuously lies in the distribution of the radiation dose. At the time of the injection of an isotope, the body content is at a maximum. It falls rapidly immediately thereafter and then more slowly with increasing time. As a result, the dose rate to which the animal is exposed at any given moment is a function of the time elapsed since administration. The dose rate also varies in space, since strontium is localized primarily in bone, and deposition occurs in those areas that are metabolically active. Distribution after a single injection is very uneven because those bone deposits that are formed when the concentration in the blood is maximal are much more radioactive than those formed when the concentration in the blood is low. Contrariwise, the intensity of the internal radiation from Sr^{90} obtained as a constant constituent of the diet is quite uniform. With continuous intake, the body burden increases rapidly at first, more gradually as equilibrium is approached, and finally it remains relatively constant regardless of time. Likewise, the spatial aspects of the dose rate vary to a much smaller degree when intake is constant because, under these conditions, consecutive metabolically active areas of bone are exposed to a relatively constant level of Sr^{90} in the blood (1).

Another difference between the administration of Sr^{90} by injection and by way of the diet deserves attention. Sr^{90} decays to Y^{90}, which has a half life of only sixty-four hours. Consequently, unless freshly separated material is used, Sr^{90} is accompanied by an almost equal amount of Y^{90} activity. The Y^{90} that is included when an equilibrium mixture is injected is deposited primarily in the organic matrix of bone and in the liver. Since it disappears quickly, however, its contribution to the total dose of radiation is relatively unimportant. About 40 per cent of the Y^{90} is excreted during the first day (2) and by the fifteenth day continuing excretion and radioactive decay decrease the amount remaining in the body to less than 1 per cent. On the other hand, when an equilibrium mixture is fed, Sr^{90} is absorbed but Y^{90} is not. As a result, the yttrium that is eaten merely passes through the alimentary tract; it is not deposited in the skeleton and the liver. Hence, ingested Y^{90} is a source of radiation only within the digestive system. In a large animal the range of the radiation does not extend far beyond the digestive tract itself. In a small animal, such as a mouse, a large part of the body is within

[1] From the Division of Biological and Medical Research, Argonne National Laboratory, Lemont, Ill. Work performed under the auspices of the U. S. Atomic Energy Commission. Presented at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15–20, 1959.

the range of an Y^{90} beta ray originating in the stomach or intestine.

In order to provide some direct information bearing on the consequences of various levels of dietary contamination, mice are being maintained on food containing Sr^{90}. The present report is an interim rather than a final evaluation of the data since many of the experimental animals are still alive.

PROCEDURES

Food Preparation: Sr^{90} at six levels is being added to commercially milled mouse food[2] before this is pelleted (see Table I). The highest level, 10 μc Sr^{90}/gm. Ca, is 10,000,000 strontium units, and the lowest 10,000 strontium units, or five times the current maximum permissible concentration for occupational exposure (3). During the first year the food was prepared by mixing the ground meal with gelatin to facilitate shaping and hardening, sodium propionate to prevent the growth of mold, a pure food dye to provide color identification, water to give the desired consistency, and Sr^{90} appropriate for the concentration of calcium in the specific shipment of ground meal. The calcium content has ranged from 1.55 to 2.06 per cent; the phosphorus content from 0.70 to 0.84 per cent. The wet mash was pushed through a converted meat grinder, which extruded the food through five tubes. After they were cut to proper length, the pellets were dried at 60 to 70° C. for forty-eight hours. Control food was prepared in the same fashion. More recently food preparation has been greatly facilitated by the use of a pelleting machine.[3] Gelatin is no longer added, the quantity of water has been reduced, and oven-drying is not required.

Animal Production and Maintenance: CF1 female mice were housed 10 per stainless steel cage and were provided with control food. One male mouse was introduced into each cage, where it was permitted to remain for twenty-four hours. This mating resulted in the control, or Level 7, mice. Nineteen days later the pregnant mice were placed individually in stainless steel boxes containing sterile wood shavings, and the remaining mice, plus additions from stock to restore the number in each cage to 10, were provided with food containing 0.01 μc Sr^{90}/gm. Ca (Level 6). Two days later the males were returned to the breeding cages, from which they were removed twenty-four hours later. The males received food containing Sr^{90} only during their stay in the breeding cages.

Nineteen days after this second breeding period the pregnant mice were isolated in confinement cages, where they continued to receive the same radioactive food. The remaining mice, plus some additions from stock, were then placed on food containing 0.1 μc Sr^{90}/gm. Ca (Level 5), and two days later the males were reintroduced into the cages. This routine was repeated, with one exception, at increasing levels of Sr^{90}, until the seven groups of mice had been bred. The exception to the routine was that the length of the mating period was increased to two and three days when Levels 1, 2, and 3 were bred, in order to increase the number of offspring that would be available for further study. The dams were approximately 110 days old when the control breeding (Level 7) began, and they were approximately 250 days old when the breeding at 10 μc Sr^{90}/gm. Ca (Level 1) took place.

The male mice and those females that did not produce litters were discarded. Thus, the experiment consists of two major groups of animals: the dams, which first received the special diet when they were from 110 to 250 days old, and their progeny, which have been exposed to radiostrontium since conception. The male offspring are being used for Sr^{90} and Ca analyses and for autoradiographic studies. These will be the subject of a separate report. The female offspring are being

[2] Rockland Mouse Diet, manufactured by A. E. Staley Manufacturing Co., Decatur, Ill.

[3] California Laboratory Pellet Mill, manufactured by the California Pellet Mill Co., 1800 Folsom St., San Francisco 3, Calif.

TABLE I: BREEDING HISTORY OF MICE FED Sr^{90}

Level	$\mu c\ Sr^{90}$ / gm. Ca	No. of Females	Litter Production		Mean No. of Young per Total Litters	
			%	%/♂-Day*	Alive at Birth	♀♀ Alive at 35 Days
1	10.0	230	17.8	5.9	8.1	2.3
2	5.0	236	8.9	4.5	7.9	2.5
3	2.5	285	16.2	8.1	8.3	2.8
4	1.0	293	6.8	6.8	7.6	2.5
5	0.1	332	12.1	12.1	8.4	2.3
6	0.01	317	12.0	12.0	7.7	1.9
7	0	319	12.5	12.5	8.8	2.6

* The males remained in the breeding cages for three days in Level 1, two days in Levels 2 and 3, and one day in Levels 4, 5, 6, and 7.

used for the long-term toxicity study (see Table II).

For five weeks the young mice remained with their mothers. At thirty-five days of age they received identifying ear marks, were grouped 15 males or females per stainless steel cage, and were supplied with food at the appropriate level of Sr^{90}. The dams were similarly caged. Experimental routine has included daily observation and monthly weighing, at which time each mouse is examined individually. Moribund animals are killed with sodium pentobarbital after a peripheral blood sample has been taken for hematological study. This procedure provides much more satisfactory material for histologic examination than can be obtained when an animal has died some time before autopsy, and it adds an observation that is often important in evaluating the terminal disease. A number of tissues are always taken for histopathologic study, and others are selected as indicated. Autopsy is followed by x-ray examination of the skeleton, after which a femur and the lumbar spine, as well as any other bones showing possible pathologic change, are taken for microscopic study.

RESULTS

I. Reproduction and Early Survival

Limitations of space and man power prevented breeding mice at all the levels of Sr^{90} at the same time. The procedure that was employed made the best use of the stock of females, and it produced all the young of a given dose level at the same time. However, because of this procedure, comparisons of reproductive capacity among the groups are not entirely valid. At each successive breeding a large part of the population consisted of females that had not bred when they had a previous opportunity to do so. However, since the "average" female mouse will mate only one day out of five, and since twenty-one days elapsed between breeding trials, it would be expected that the mice in estrus at any period would not have been receptive at a previous period. Another reason for caution in comparing the groups for reproductive capacity is that the Level 1 mice were bred four months after the Level 7 mice, and a period of four months is a significant portion of the reproductive life of a mouse. Furthermore, seasonal variations in reproductivity have been observed in this species, and manifestations of endemic disease within a mouse colony often fluctuate in severity from time to time.

The data in Table I should be examined with these reservations in mind. Variations in the percentages of females that produced litters and in the average number of live young per total number of litters were probably due to an endemic intestinal infection which became apparent soon after the first litters were born. A few lactating mice became ill and failed to care for their young. A short time later some mice in the breeding cages exhibited similar symptoms, including pallor, lethargy, and diarrhea; they did not have offspring.

TABLE II. POPULATIONS COMPRISING THE LONG-TERM TOXICITY STUDY

Level	$\mu c\ Sr^{90}$ / gm. Ca	Number of Dams	Number of Females Raised on Sr^{90}
1	10.0	37	95
2	5.0	21	53
3	2.5	46	129
4	1.0	20	49
5	0.1	38	94
6	0.01	31	71
7	0	31	105

The average litter size was large. There were 11 or more young in many litters, and even 15 in a few. The number of mice per litter did not seem to be influenced by the level of Sr^{90} in the diet nor by the age of the parents. The number of females reared to 35 days of age also did not appear to be correlated with the concentration of Sr^{90} in the food. However, an average of only 2.4 females per litter reached 35 days of age. Since the average litter consisted of 8.1 young at birth, there should have been an average of 4 females. This loss of an average of 1.6 females per litter between birth and 35 days of age was due primarily to the infection mentioned above. The male young were excluded from this survey because many of them had been removed for analysis or autoradiography.

II. Evaluation of the Data at 525 Days

The 224 dams and their 596 female offspring that reached 35 days of age are listed in Table II according to the concentration of Sr^{90} in their diets. The present report includes the observation up to 525 days after the last mice were born.

The Dams: Only those mice that have been maintained on the highest level of dietary Sr^{90} since they were 110 to 250 days old have shown any evidence of injury during the first 525 days of the experiment. A decrease in survival was first apparent at about 450 days of age, and this has become more pronounced with time. Since the dams entered their final experimental groups at different ages, the survival data are referred to absolute age rather than to days on the Sr^{90} diet in Figure 1. The

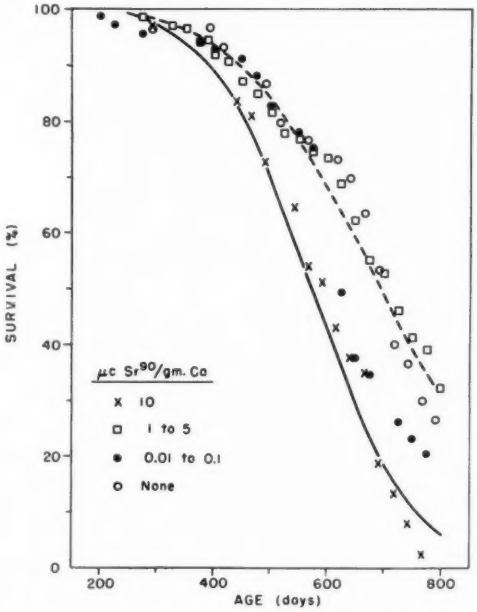

Fig. 1. Survival of CF1 female mice maintained on food containing Sr^{90} after they were 110 to 250 days old.

curves are replotted from a straight-line fit of the data graphed on an arithmetic probability grid. The survival data are not smooth because of the endemic disease discussed earlier and because of an additional acute intestinal infection that appeared among the Level 5 dams when they were about 600 days old. In spite of the variability of the data due to these diseases, it can be seen that survival has been markedly decreased by a diet containing 10 $\mu c\ Sr^{90}$/gm. Ca but not by diets containing 5 $\mu c\ Sr^{90}$/gm. Ca or less. The interpolated median survival time for the Level 1 mice is 575 days of age; for all the other groups, including the controls, it is 695 days.

There have been no osteogenic sarcomas among these mice, nor any of the other neoplasms of bone that have been observed in CF1 female mice after the injection of Sr^{90} (4). Particular attention has been given to tumors of the blood-forming tissues since these diseases occurred earlier among mice injected with Sr^{90} than among their controls (4, 5). The frequency dis-

TABLE III: AVERAGE BODY WEIGHT OF MICE REARED ON Sr^{90}

Level	$\mu c\ Sr^{90}$ / gm. Ca	35 Days of Age		98 Days of Age		190–197 Days of Age		393–414 Days of Age	
		No. of Mice	Weight (gm.)	No. of Mice	Weight (gm.)	No. of Mice	Weight (gm.)	No. of Mice	Weight (gm.)
1	10.0	95	15.1	88	22.5	81	25.5	52	28.6
2	5.0	53	16.5	52	21.5	51	24.3	37	26.3
3	2.5	129	14.2	125	20.5	120	23.3	85	27.5
4	1.0	45	16.6	45	24.7	43	26.6	27	29.5
5	0.1	90	14.0	86	23.2	84	25.0	72	27.8
6	0.01	71	12.7	70	23.6	67	27.3	60	26.4
7	0	105	15.3	103	23.7	101	26.2	87	28.8

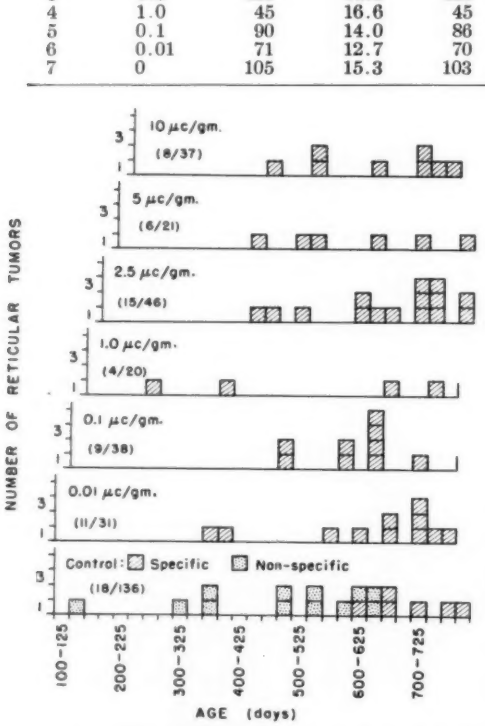

Fig. 2. Frequency distribution of deaths with tumors of the blood-forming tissues among the mice maintained on food containing Sr^{90} after 110 to 250 days of age. The specific controls are the Level 7 dams; the nonspecific controls are the Level 7 female offspring.

tributions of these reticular tissue tumors are presented in Figure 2. There is no evidence that they have appeared earlier among the mice receiving Sr^{90} in their food, and there is only a slight suggestion that they may be occurring in greater number. An accurate evaluation of tumors of the blood-forming tissues in CF1 female mice requires that they be classified according to cell type, and histologic examination has not been completed. In this strain only the lymphocytic neoplasms appear to be influenced by radiation (6), and these cannot be differentiated from the other tumors of the blood-forming tissues at gross autopsy.

The Mice Reared on Sr^{90}: By 100 days of age the mice that had been maintained on 10 μc Sr^{90}/gm. Ca since conception were dying at a more rapid rate than the others, and by 300 days of age it was apparent that concentrations of 5.0, 2.5, and 1.0 μc Sr^{90}/gm. Ca in the diet also were detrimental. The survival data are presented in Figure 3; the curves were drawn from the values estimated from an arithmetic probability plot of the data. Although there has been some variability in survival associated with the endemic infection that has plagued this experiment, it is clear that a dietary concentration of 1.0 μc Sr^{90}/gm. Ca or higher has resulted in a shortening of the life span. Apparently 0.1 and 0.01 μc Sr^{90}/gm. Ca had no effect on survival during the first 525 days. The median survival times estimated from the curves are 405 days for Level 1, 510 days for Levels 2, 3, and 4, and 685 days for Levels 5, 6, and 7.

Body weights have not reflected the deleterious effects of food containing Sr^{90} (Table III). There have been some variations associated with the endemic disease, but the average body weights have shown no consistent differences among the seven populations. The variability decreased as the mice became older and as the chronically ill animals died. For example, Level 6 mice at 35 days of age, when they had a high incidence of diarrhea, weighed on the average only 83 per cent as much as the control mice, but when they were about 400 days old their average weight was almost 92 per cent that of the controls.

Ten μc Sr^{90}/gm.Ca in the diet was associated with an early appearance of a large number of tumors of the blood-forming tissues (Fig. 4). Many of the early tumors that have been examined histologically have been classified as lymphomas. By 525 days of age 24 per cent of the Level 1 mice, but only 6 per cent of the control mice, had died with reticular-tissue tumors. By 650 days the

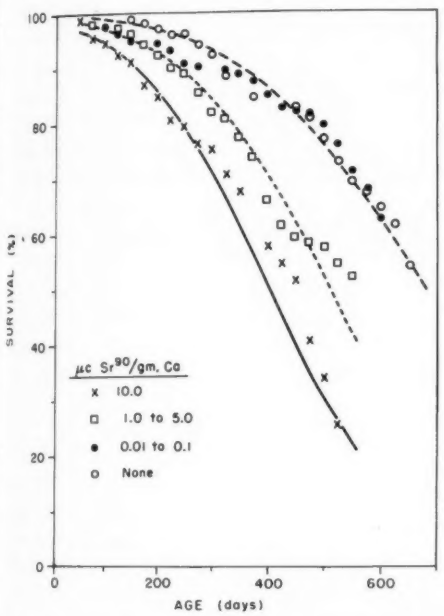

Fig. 3. Survival of CF1 female mice exposed to Sr^{90} since conception.

percentage among the control mice had risen to 11 per cent. At present there is no indication that lower concentrations of Sr^{90} in the diet have influenced the incidence of these neoplasms.

In addition to the tumors of the blood-forming tissues, there have been 12 other malignant tumors among the Level 1 mice that can be attributed to Sr^{90}. All were found in animals that were autopsied between 450 and 525 days of age. Six have been tentatively diagnosed as osteogenic sarcoma, 4 as osteolytic tumors, and 2 as epidermoid carcinoma of the oral cavity. No similar neoplasms had appeared by 525 days among any of the other groups of mice.

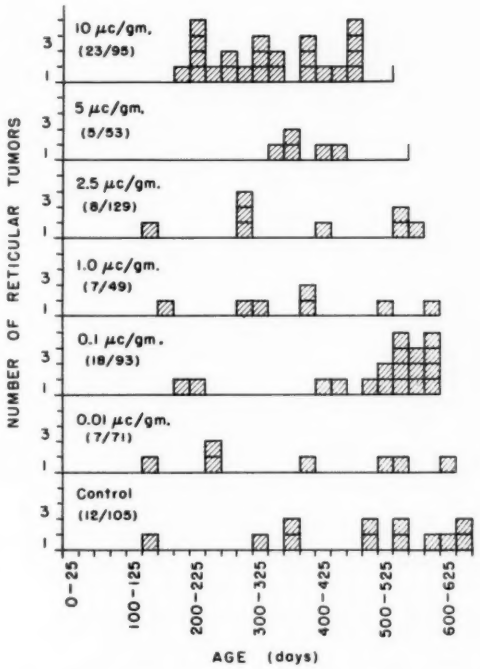

Fig. 4. Frequency distribution of deaths with tumors of the blood-forming tissues among mice exposed to Sr^{90} since conception.

DISCUSSION

The internal dose of radiation from Sr^{90} that is acquired by eating contaminated food day after day is delivered evenly in time. Once equilibrium has been reached between the amount ingested and the amount excreted, the body burden remains constant. The spatial distribution of the radiation dose is also as uniform as possible when exposure is through continuous ingestion. Since strontium is localized in the skeleton, however, the dose rate throughout the entire body cannot be the same. Nor is it completely uniform even within the skeleton since strontium is deposited almost exclusively in mineralized bone. The uniformity of the radiation dose increases as the range of the ionizing particles increases; it also increases as the size of the object being irradiated de-

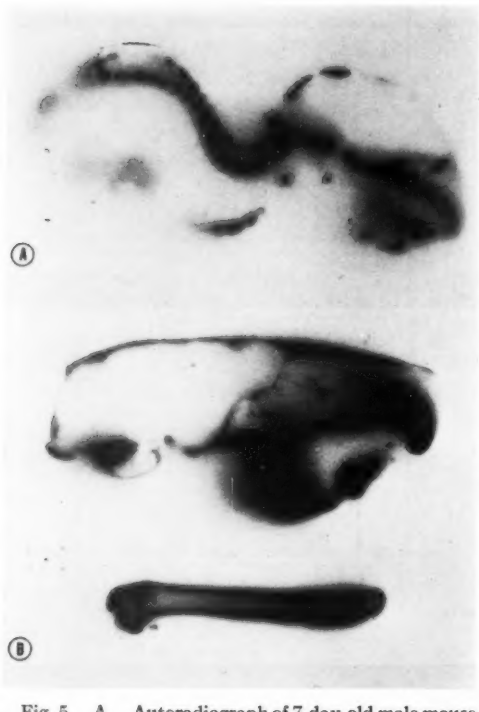

Fig. 5. A. Autoradiograph of 7-day-old male mouse of Level 1 (10 μc Sr^{90}/gm. Ca). B. Autoradiographs of skull and femur of 407-day-old male mouse of Level 1.

creases. Since the bones of mice are quite small relative to the range of the beta particles resulting from Sr^{90}-Y^{90} decay, the spatial distribution of the dose of radiation is fairly uniform in this species. For example, a mouse femur is somewhat less than 1.5 mm. in diameter, and the cortex is about 0.12 mm. thick. On the other hand, the maximum range in bone of the Sr^{90}-Y^{90} beta particles is approximately 5.5 mm., and the average range is 1.3 mm. However, even under these optimum conditions for obtaining a uniform dose rate in space, a considerable range of intensity exists, as evidenced by the autoradiographs presented in Figure 5. It is important to keep this situation in mind, particularly when mouse data are extrapolated to larger animals and to man. For example, the dose received by the marrow of a mouse femur, which is suggested by the graying in this area in Figure 5 B, cannot be related directly to the dose that might be received by the marrow in the femur of a dog or man.

The method of preparing the Sr^{90} food was not satisfactory during the first year of the experiment, and there was some concern that certain nutrients might be destroyed during the long drying period at 60–70° C. Also, it was feared that the endemic intestinal infection, which became apparent early in the course of the experiment, might invalidate the results. It was possible, of course, that the disease itself was related to a nutritional deficiency. Neither the severity of the disease nor the number of animals involved seemed to be associated with the concentration of Sr^{90} in the diet. In spite of these early difficulties, the estimated median survival times of most of the groups are longer than the average life spans of CF1 female mice that have served as controls in other experiments (7).

It had been anticipated from experience with injected Sr^{90} that Levels 1 through 4 would have much more serious consequences than have been observed to date. Among the dams damage has been seen only at Level 1 (10 μc Sr^{90}/gm. Ca). There has not been an increase in neoplastic disease, but the median life span appears to be decreased by about 17 per cent. The mice that have been maintained on Level 1 food since conception show a decrease in median life span of about 41 per cent; those on Levels 2, 3, and 4 food show a reduction of about 26 per cent. In none of these groups, however, does the growth rate appear to have been affected, and there has been no gross evidence of radiation damage in the digestive tract. Tumors attributable to radiation appeared by 525 days only among the mice that have been exposed to the highest concentration of Sr^{90} since conception.

The greatest difference between expectation and observation concerns osteogenic sarcomas. Since in other experiments the shortest interval between the injection of a 70-day old mouse and its death with a malignant bone tumor has been about

150 days (8), and since it is generally assumed that young tissues are more radiosensitive than mature ones, the absence of these neoplasms until the animals had reached 450 days of age was unexpected. Also, it had been estimated that the incidence of osteogenic sarcomas among the mice reared on Level 1 food would be well above 50 per cent. This prediction was derived as follows. An adult female mouse weighs about 30 gm. and approximately 1 per cent of its body weight, or 0.3 gm., is calcium. With constant exposure to 10 μc of Sr^{90} for each gram of Ca, therefore, the animal should contain between 1.5 and 3 μc of Sr^{90}, depending upon the degree of metabolic discrimination against strontium (9), by the time it weighs 30 grams. This is equivalent to a body burden of 0.05–0.1 μc/gm. The average CF1 female mouse lives about 600 days, and the retention of injected Sr^{90} is about 11 per cent at 600 days (4). Consequently, a body burden of 0.05–0.1 μc/gm. would be expected 600 days after the injection of 0.45–0.91 μc/gm. The injection of mice with such amounts of Sr^{90} has been followed by osteogenic sarcoma in 80 to 100 per cent (4).

There have been only 6 osteogenic sarcomas among the mice that have been maintained since conception on 10 μc Sr^{90}/gm. Ca. This group consisted initially of 95 mice; 86 were alive at 150 days of age, and 48 remained at 450 days, when the first death with an osteogenic sarcoma occurred. Twenty-four mice are still alive at 525 days. Since 6 of the last 24 that died had osteogenic sarcomas, a reasonable guess would be that 6 of the remaining 24 also will have osteogenic sarcomas. This would bring the final number to 12 tumor-bearing mice out of the 95 mice weaned (13 per cent) or 12 out of the 48 mice alive when the first tumor death occurred (25 per cent). Very likely the difference between these values and the original estimate of 80 to 100 per cent is due to the absence of the initial high dose rate that immediately follows an injection. Variations of the dose rate in space probably are not of great importance in this case because the mouse skeleton is so small relative to the range of the Sr^{90}-Y^{90} beta particles. There is additional evidence from several other recent experiments that the dose rate is a significant factor in radiocarcinogenesis and that the neoplastic response is not dependent exclusively upon the total energy absorbed (1, 6, 10).

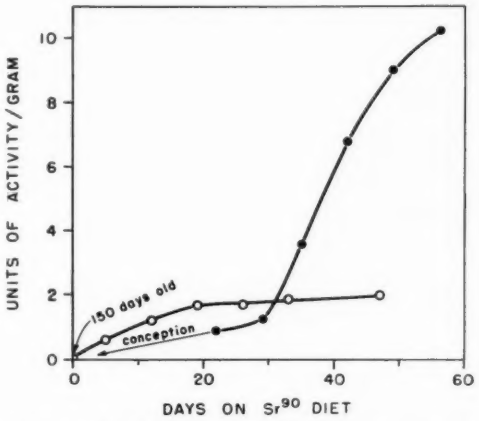

Fig. 6. Relative amount of radioactivity per gram mouse as a function of age and duration of exposure to food containing Sr^{90}.

Although there have been no osteogenic sarcomas in any of the other groups of mice, it is possible that some will appear among the animals that are still alive. However, even if there are a few neoplasms at lower levels, information at higher concentrations will be required to delineate dose-response relationships. Consequently, the experiment is being extended to include a diet containing 15 μc Sr^{90}/gm. Ca. This should be within the carcinogenic range for animals exposed from conception to death, but it probably will not be carcinogenic for the dams. The data presented in Figure 6 show that the body burden of mice that were first exposed to a diet of Sr^{90} when they were 150 days old approached equilibrium in about 20 days. The total radioactivity per gram body weight of these mice after they had been on the diet for 50 days was very much lower than that of mice that had been maintained on the

same concentration of Sr^{90} from the time of conception. These preliminary data suggest that, by the time equilibrium has been reached by both groups of mice, those that have always been exposed to radiostrontium will have about ten times as much activity per gram of body weight as those that have been exposed only since they were 150 days old. Consequently, food containing 100 μc Sr^{90}/gm. Ca would be required to bring an adult mouse to the same body burden as that of a mouse that had been exposed to 10 μc/gm. Ca throughout life. It should be pointed out that these carcinogenic concentrations of Sr^{90} in the diet of mice are enormous compared with the current level of contamination of human food from fall-out.

SUMMARY

Two groups of mice are being maintained on food containing Sr^{90}. The first was placed on the special diet at 110 to 250 days of age, and this group produced the second, which has been exposed to Sr^{90} since conception.

Levels of dietary Sr^{90} as high as 10μc/gm. Ca did not adversely affect conception, parturition, or lactation. The median survival time of the dams maintained on this level of Sr^{90} for 525 days, however, was reduced by about 17 per cent. Dams maintained on 5μc Sr^{90}/gm. Ca or less did not differ substantially from the control mice in survival time or in disease incidence during these 525 days.

The median life span of mice exposed to 10 μc Sr^{90}/gm. Ca since conception was reduced by about 41 per cent. A decrease in survival time was also apparent among the mice reared on 5.0, 2.5, and 1.0 μc Sr^{90}/gm. Ca.

Tumors that can be attributed to radiation have appeared only among those mice maintained throughout life on 10μc Sr^{90}/gm. Ca. Besides an increase over the normal incidence of tumors of the blood-forming tissues, there have been epidermoid carcinomas of the oral cavity, osteolytic tumors of the skeleton, and osteogenic sarcomas.

The osteogenic sarcomas appeared much later and in much smaller number than had been expected on the basis of previous experience with mice that had been injected with Sr^{90}. Since the major difference between a single injection and continuous ingestion concerns the dose rate, it appears that the amount of radiation absorbed per unit time is an important factor in the neoplastic process. In addition, the delay in the appearance of osteogenic sarcomas until the mice were approximately 450 days old suggests that very young mice are not necessarily more sensitive to a radiocarcinogenic stimulus than adult mice.

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SUMMARIO IN INTERLINGUA

Le Consequentias del Continue Ingestion de Sr^{90} per Muses

Con le objectivo de determinar le responsa de animales laboratorial al ingestion continue de micrissime quantitates de Sr^{90}, duo gruppos de muses es mantenite con dietas continente le mentionate elemento radioactive. Le prime gruppo esseva mantenite con le dieta special durante le intervallo de etate ab 110 usque a 250 dies, e iste gruppo produceva le secunde que se trova exponite a Sr^{90} depost le conception. Viste que multes del animales experimental vive ancora a iste tempore, le presente reporto include solmente le observationes colligite usque a 525 dies post le nascentia del ultime muses ancora includite e debe esser considerate como un evalutation interime plus tosto que final del datos.

Concentrationes dietari de Sr^{90} usque al nivello de 10 μc per g de Ca non exerceva un effecto adverse super le conception, parturition, o lactation. Tamen, le superviventia median del matres mantenite a iste nivello de radioactivitate durante 525 dies esseva reducite per circa 17 pro cento. Matres mantenite a 5 μc de Sr^{90} per g de Ca o minus non differeva notabilemente ab le muses de controlo in lor longevitate o in le incidentia de morbiditate durante iste intervallo.

Le longevitate median de muses exponite a 10 μc de Sr^{90} per g de Ca a partir del conception esseva reducite per circa 41 pro cento. Un reducite longevitate esseva etiam evidente inter le muses elevate con 5,0, 2,5, e 1,0 μc de Sr^{90} per g de Ca.

Tumores que pote esser attribuite a radiation ha apparite solmente in muses mantenite durante lor integre vita a 10 μc de Sr^{90} per g de Ca. A parte le augmento, comparate con le incidentia normal, in le numero del tumores de tissu hematopoietic, le sequentes esseva incontrate. Carcinoma epidermoide del cavitate oral, tumor osteolytic del skeleto, sarcoma osteogene.

Le casos de sarcoma osteogene se declarava multo plus tardivemente e in numeros multo plus basse que lo que habeva essite expectate super le base de previe experientias con muses a que injectiones de Sr^{90} esseva administrate. Proque le major differentia inter un sol injection e le ingestion continue es un question de dosage, il pare que le quantitate de radiation absorbite in le unitate de tempore es un factor importante in le processo neoplastic. In plus, le retardo in le apparition del sarcomas osteogene usque al tempore quando le muses habeva approximativemente 450 dies de etate suggere que juvene muses non esseva necessarimente plus sensibile al stimulo radiocarcinogenetic que muses adulte.

Pyeloureteritis Cystica

Report of a Case with Spontaneous Rupture of the Ureter[1]

JOHN E. SHICK, M.D., and JAMES J. SHEA, M.D.[2]

THE ROENTGEN diagnosis of pyeloureteritis cystica was first reported in 1929, by Joelson (1) in America and Jacoby (2) in Germany. Since that time further cases have been published mainly in the surgical literature (3). Only a few reports have appeared in the English-language radiological journals (4–7).

The following case is of interest not only as illustrating the condition but also because of the unusual finding of spontaneous rupture of the ureter with extravasation. This complication, so far as we know, has not been previously reported in the radiological literature.

CASE HISTORY

A 45-year-old man was admitted to the hospital with a history of two severe attacks of ureteral colic, one at 3 P.M. the day prior to entry and the second during the night. The pain radiated to the left testis and left flank and was associated with frequency, gross hematuria, and nausea. There had been no previous attacks.

A plain film of the abdomen showed a calculus overlying the left sacroiliac joint (Fig. 1). A retrograde pyelogram the following day (Fig. 2) showed the stone still unchanged in position and revealed a typical beaded area in the upper ureter and pelvis of the kidney. The retrograde pyelogram was done by the bulb method, and the catheter was never introduced beyond the lowermost portion of the ureter. Intravenous pyelography two days later (Fig. 3) showed the stone 1 cm. lower than in the original view. The striking feature, however, was the extravasation of contrast material along the upper ureter as a result of spontaneous rupture.

A ureterolithotomy was done and the retroperitoneal tissue was found to be edematous and inflamed, with evidence of extravasation of fluid in this area. There was also severe edema of the ureteral wall, but no distinct area of perforation was found. A ureterostomy was done below the renal pelvis and a catheter passed upward and downward in the ureter to confirm the impression that it contained no specific rent. The stone was then removed. A T-tube was placed through the superior ureterostomy and a catheter was inserted, being passed beyond the inferior ureterostomy into the bladder. The patient made an uneventful recovery, and an intravenous pyelogram two weeks later (Fig. 4) showed patency and continuity of the ureter without evidence of extravasation. There was some slight undulating irregularity of the upper ureter, probably due to residual cysts.

DISCUSSION

Pyeloureteritis cystica is usually associated with infection. Of 57 cases reported by Loitman and Chiat (4), 52 showed definite evidence of urinary tract infection. Concomitant pyelonephritis may occur. The pathogenesis of the cysts has been explained by von Brunn (8) on the basis of degeneration of central cells in epithelial nests beneath the mucous membrane. These nests develop from downward proliferation of the surface epithelium as a result of inflammation and become detached from the mucous membrane. It is the protrusion of these cysts into the lumen of the ureter and pelvis which causes the lucent defects and scalloping seen on the radiograph. It is probable that in the case reported extension of the cysts through the muscular coat and adventitia was the cause of the extravasation.

Diagnosis can be made from the intravenous pyelogram, but retrograde pyelograms show the cysts to better advantage. They are located in the upper third of the ureter and pelvis and are multiple. Differentiation from other conditions seldom offers any great problem. Multiple papillomas tend to occur in the lower ureter. Nonopaque stones are single or few in number and mobile. Air bubbles in retrograde studies are quite sharp, smooth and circular.

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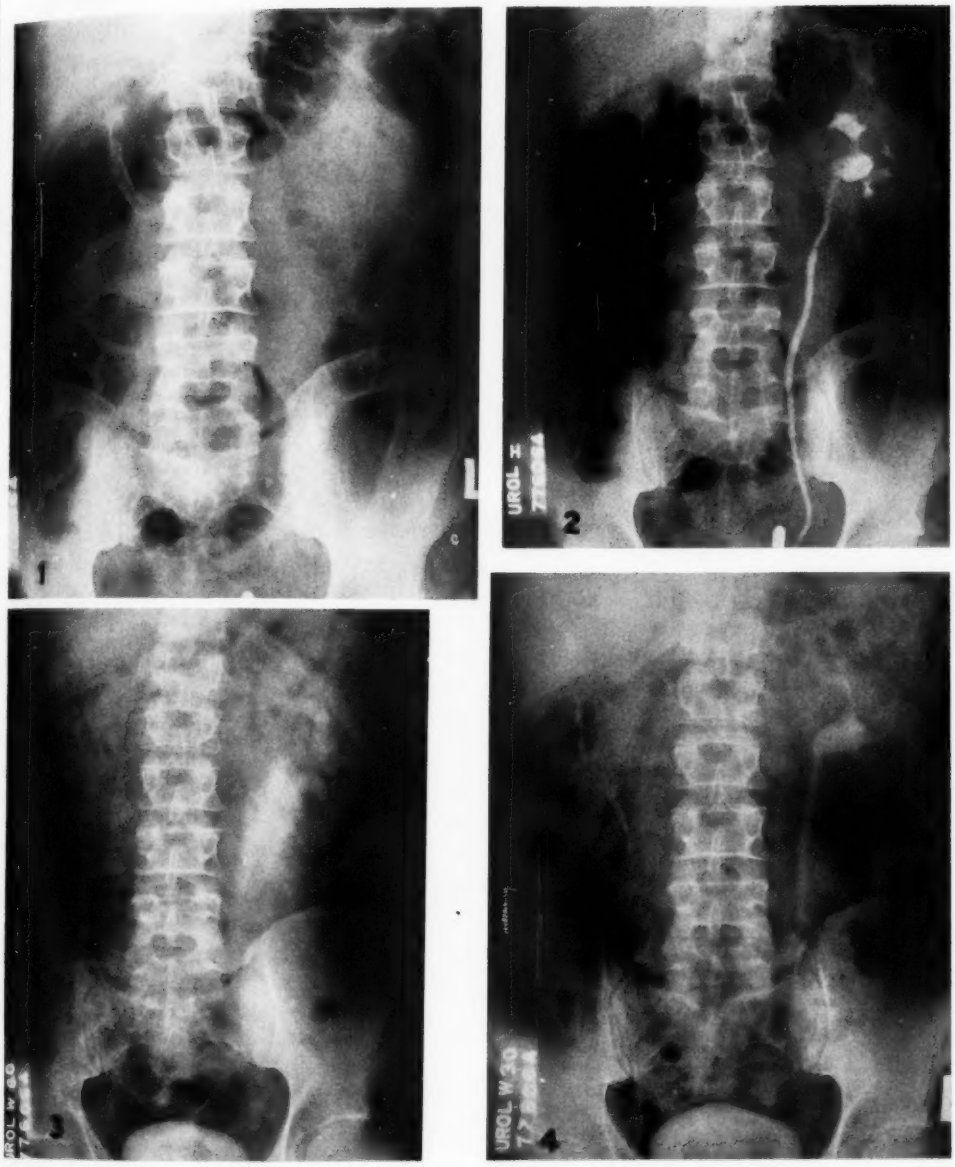

Fig. 1. Stone in lower ureter, Oct. 14, 1958.
Fig. 2. Retrograde pyelogram demonstrating cystic changes in the upper ureter and pelvis, Oct. 15, 1958.
Fig. 3. Intravenous pyelogram showing extravasation of contrast medium, Oct. 17, 1958.
Fig. 4. Postoperative intravenous pyelogram showing patency and continuity of the ureter, with slight residual change in its upper course, Oct. 30, 1958.

and move within the ureter; they should cause no uncertainty on intravenous pyelography. Blood clots are larger and more irregular in shape. Small pedunculated tumors in the pelvis and tuberculous granulations may be difficult, if not impossible, to distinguish radiologically from pyeloureteritis cystica.

SUMMARY

A case of pyeloureteritis cystica with spontaneous rupture has been presented. Removal of a ureteral stone resulted in cure of the secondary cystic changes.

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SUMMARIO IN INTERLINGUA

Pyelo-Ureteritis Cystic: Reporto de un Caso con Ruptura Spontanee del Uretere

Es reportate un caso de pyelo-ureteritis cystic, complicate per un ruptura spontanee del uretere e extravasation del substantia de contrasto al longo de su curso superior. Pyelographia retrograde demonstrava un calculo in le uretere inferior e alterationes cystic in le uretere superior e le pelve. Un pyelogramma intravenose, effectuate duo dies plus tarde, demonstrava le substantia extravasate. Al operation il esseva trovate que le pariete ureteral esseva edematose, sed nulle distincte area de perforation esseva discoperite. Es opinate que un extension del cystes a transverso le strato muscular e le tunica adventitie esseva responsabile pro le extravasation. Le alterationes cystic dispareva post le elimination del calculo.

Myelolipoma of the Mediastinum[1]

HERMAN LITWER, M.D.

MYELOLIPOMAS are uncommon tumor-like masses composed of heterotopic bone marrow and adipose tissue. They are incidental findings, and their pathological significance is obscure. While they usually occur in the adrenal glands, a few cases have been reported in other parts of the body, mainly in the retroperitoneal area but occasionally also in the chest (3, 4, 8). Though they may be without demonstrable relation to other disease, they are sometimes found in association with severe anemias (1, 2, 5–7). In such cases they have been thought to represent a manifestation of compensatory hematopoiesis. Extramedullary hematopoiesis is not uncommon in severe anemias, but the areas of heterotopic bone marrow, though usually found in fatty tissue (particularly in the retroperitoneal region), only rarely take the form of discrete tumor-like masses (9).

Myelolipomas differ from mesenchymomas and teratomas in that they are composed only of fatty tissue and heterotopic bone marrow, without other elements. It is questionable whether they should be classified as true tumors.

A review of the literature revealed only a few reports of mediastinal myelolipomas, and these were discovered postmortem (2, 4, 5, 7, 8). No case could be found in which the mediastinal mass was demonstrated roentgenologically. In 2 cases of congenital hemolytic jaundice (hereditary spherocytosis) coming under our observation, mediastinal masses apparent on the chest films proved to be myelolipomas.

CASE REPORTS

CASE I: W. L. H., a 63-year-old white man, was admitted to the Veterans Administration Center on Oct. 31, 1953, complaining of abdominal pain, gradually increasing since the preceding May, severe headaches since 1918, and urinary difficulties. In 1918 he had suffered an attack of jaundice of undetermined origin and since that time had exhibited jaundice of varying degree, with acholic stools He had a cholecystectomy and appendectomy in 1924 and was studied extensively in several hospitals between 1924 and 1933. The main finding was a chronic anemia of unusual type.

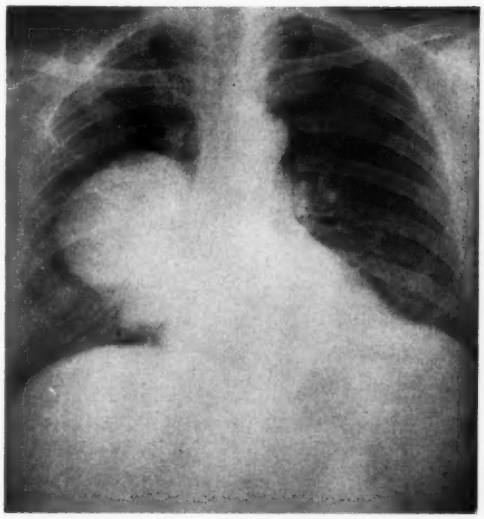

Fig. 1. Case I. Large mediastinal mass in right middle and lower fields.

Films obtained in 1927 were unavailable but were reported (Dr. Meinhart and Dr. Christie) as showing a large dense bilobate shadow in the chest, extending from the mediastinum toward the right and left, at the level of the eighth, ninth, and tenth ribs, overlapping the heart shadow. It suggested some kind of tumor. A gastrointestinal series showed a raggedness of the greater curvature of the stomach, near the cardia, thought to be due to pressure by the colon.

On a repeat x-ray examination in 1933 the shadow in the chest was found to have increased in size and was interpreted as enlarged lymph nodes.

During hospitalization in 1953 a diagnosis of congenital hemolytic anemia was made.

Radiological examination of the chest (Fig. 1) now showed a homogeneous, somewhat lobulated shadow extending from the right posterior mediastinum into the right middle and lower lung field, measuring 13 cm. in its greatest diameter. There was a smaller homogeneous paravertebral shadow in the left lower

[1] From the Department of Radiology, Veterans Administration Center, Martinsburg, W. Va. Accepted for publication in March 1959.

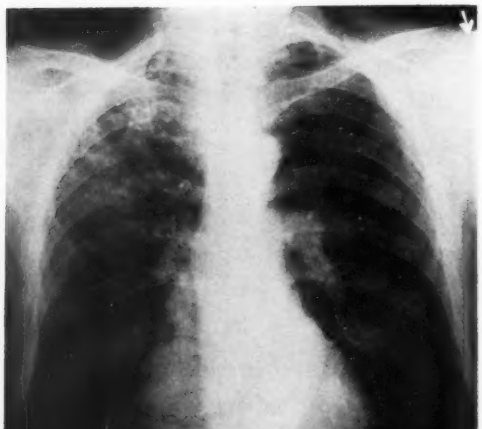

Fig. 2. Case II. Mediastinal masses in both lower fields. There is an old tuberculous process in the right upper lobe.

mediastinum. A gastrointestinal series showed an irregular, scalloped filling defect on the upper portion of the greater curvature with fairly smooth margins.

Bronchoscopy was reported as demonstrating some narrowing of the right main-stem bronchus, as if by extrinsic pressure on its anterior lateral wall.

Needle biopsy of the mediastinal mass was not diagnostic. Biopsy of a lymph node from the right side of the neck showed lymphadenitis with reticular hyperplasia. On bone marrow puncture the findings were compatible with malignant disease.

On gastroscopy several rounded elevations, approximately 1.5 cm. in diameter, were seen, having the appearance of intramural benign neoplasms. The mucous membrane was normal.

The consensus of opinion was that the mediastinal shadows represented neurofibromas and that the changes of the stomach were due either to neurofibromas (this possibility was entertained because of the 1927 report), or to an entirely different condition of unknown origin.

Exploratory laparotomy was refused and the patient died Feb. 15, 1954.

At autopsy paravertebral masses were found in the right and left lower mediastinum. The mass on the right side, 9 × 8 cm., filled the inferior half of the costovertebral gutter. It was covered by a fibrous capsule and attached medially to the lateral aspect of the spine by a short broad stalk. The center was meaty, dark red, and somewhat spongy, resembling slightly the cut surface of a congested spleen.

Microscopically, the mass consisted of adipose tissue cells and hematopoietic cells in varying proportions. It did not contain any other tissue elements. The pathological diagnosis was myelolipoma (Dr. R. G. Gottschalk).

Other autopsy findings were carcinoma of the stomach and changes in the spleen characteristic of hereditary spherocytosis.

CASE II: G. W. F., a white male 62 years old, was admitted to the Veterans Administration Center on Sept. 3, 1956, complaining of loss of weight and energy and progressive shortness of breath for the past month. His complexion was somewhat sallow. He had signs and symptoms of chronic anemia. A cholecystectomy had been done in 1951, and a lipoma had been removed from the left arm. Two sisters had undergone splenectomy for anemia.

During the patient's stay in the hospital, a diagnosis of hereditary spherocytosis was made.

Radiological examination of the chest (Fig. 2) showed an old fibro-calcific tuberculous process in the right upper lobe. In addition, there were sharply defined densities in the posterior mediastinum on both sides of the midline, merging with the shadow of the lower mediastinum. On the right side, the density seemed to be a conglomerate mass with a lobulated appearance. On the left there was little lobulation and the long axis of the shadow was parallel to the spine. No pulsation of the masses was observed on fluoroscopic examination; there was no change in size during the Valsalva test, and no significant change of position in relation to the posterior ribs on inspiration and expiration. The dorsal vertebrae were not eroded. The esophagus was normal and appeared unrelated to the mediastinal shadows. There was no herniation of the stomach or bowel above the diaphragm. Planigrams showed the abnormal areas to be of homogeneous density without calcification. The radiological impression was lipofibromas or neurofibromas.

Bronchoscopy was negative.

Thoracotomy showed a large mass in the right lower posterior mediastinum, measuring 7 × 6.5 × 3 cm. It was attached to the lateral aspect of the vertebrae but could be easily resected. The outer surface was moderately dense, glistening, slightly bosselated and covered by a thin, smooth, glistening capsule. In one area a small amount of adipose tissue was attached. The mass was deep reddish purple, extremely uniform, and very soft.

The microscopic picture was essentially similar to that of bone marrow, with a variable proportion of adipose tissue cells. In some areas, marrow cells were few and about three-quarters of the tissue consisted of adipose tissue cells. Elsewhere marrow cells were abundant and adipose tissue cells rare, representing less than one-tenth of the cut surface.

The pathologic diagnosis was myelolipoma (Dr. R. G. Gottschalk).

SUMMARY

Two cases of myelolipoma of the mediastinum are reported. Both were associated with congenital hemolytic anemia (hereditary spherocytosis). In both, the masses of heterotopic bone marrow and adipose tissue were demonstrable on the chest film. They had evidently produced no deleterious effects. In one case the myelolipomas had been present for at least twenty-five years without significant change.

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SUMMARIO IN INTERLINGUA

Myelolipoma del Mediastino

Myelolipomas, de occurrentia pauco commun, es massas tumoroide componite de heterotopic medulla ossee e tissu adipose. Illos occurre le plus frequentemente in le glandulas suprarenal sed es trovate occasionalmente in altere sitos. Ben que illos pote apparer sin demonstrabile relation con altere morbos, illos ha essite incontrate in association con anemia sever.

Es reportate duo casos de myelolipoma del mediastino. Ambes esseva associate con congenite anemia hemolytic (spherocytosis hereditari). In ambes, le massa de heterotopic medulla e tissu adipose esseva visualisate in le roentgenogramma thoracic. Illo evidentemente habeva causate nulle effecto adverse. In un del casos, le myelolipoma habeva essite presente durante al minus vinti-cinque annos sin manifestar ulle significative alteration.

A Comprehensive Radiation Control Program in New York City[1]

HANSON BLATZ[2]

FOR MANY YEARS THE Board of Health, which is the legislative body concerned with health affairs in New York City, and the Department of Health, which administers the protective health services, have been interested in the problem of protecting citizens against ionizing radiation. Early efforts were directed to shoe-fitting fluoroscopes. These were put under permit in 1948, at which time they were regulated by the Board of Health, and inspectors were trained to supervise their operation, maintenance, and use.

With the greater realization of potential dangers in ionizing radiation, both the Board and the Department began to study the problem more intensively. Activities of the Atomic Energy Commission in New York City in policing radioisotopes were reviewed, as was the problem of transportation of radioactive material within the city. It was finally decided that the City Health Code should have a special section concerning radiological hazards. At the same time, the New York State Department was working on the problem and passed a code applicable to the rest of the State. The State Department of Labor also developed state-wide regulations.

A mandatory registration system was set up by the City Health Department and became part of the law on March 19, 1958. At that time, the Department had a small radiological control unit made up of a number of sanitarians whom it had begun to train in 1950. It was not, however, until early in 1959 that a group of highly trained persons under the direction of an experienced radiological specialist was established.

Because many different city agencies were developing radiation control programs, the Mayor's Advisory Committee recommended that responsibility for overall planning and co-ordination be placed under the direction of a single person who would work within the framework of the Department of Health.

THE CODE

The Radiation Code Health was widely circulated and public hearings were held for its discussion. It was passed, becoming effective June 15, 1958. The Code provides for the registration of all radiation sources within New York City and requires compliance with recommendations of the National Committee on Radiation Protection (N.C.R.P.). There is a registration fee of $15.00 for the first two years and a subsequent $10.00 biennial re-registration fee.

OFFICE OF RADIATION CONTROL

An Office of Radiation Control was established but, before a program could be adopted, a study was necessary to determine the most effective means of meeting the city's various radiation problems. An Advisory Committee on Radiation was accordingly appointed by the Mayor, with Dr. John C. Bugher of the Rockefeller Foundation as Chairman and a membership including radiologists, radiological physicists, a dentist, and representatives of industry and health insurance, all of whom are experts in some area of radiation use.

The Director of the Office of Radiation Control, in addition to being Scientific Secretary to the Mayor's Advisory Committee, serves as consultant to the Interagency Council on Radiation. This Council is made up of representatives of all

[1] Presented at the Forty-fifth Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 15–20, 1959.

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city agencies whose activities in any way relate to radiation or radioactive materials. These include the various public safety, water supply, and sanitation agencies.

PRE-PROGRAM STUDY

Before any program was decided upon, all available existing Radiation Control Programs were studied, including that of the Atomic Energy Commission, those of various state agencies, and that of the U. S. Public Health Service. Applicable recommendations of the National Committee on Radiation Protection were listed and evaluated with respect to the degree of overexposure that could occur if these were not heeded, and the number of individuals likely to be overexposed. It soon became apparent that by far the greatest problem concerned the use of medical and dental x-ray equipment. This was borne out by a review of the reports of the National Academy of Sciences issued in 1956 and of the United Nations Scientific Committee on Radiation, and was confirmed by testimony before Congressional hearings (Fig. 1).

Observations made in hospitals, clinics, and physicians' and dentists' offices showed that, of the recommendations of the National Committee which were not being generally observed, only a small number were of importance for control of overexposures to either patients or operators of equipment.

The radiation control problem in New York City is twofold. One part consists in administration of the Health Code to make certain that radiation workers, medical and dental patients, and the general population are not being unnecessarily exposed routinely to radiation and radioactive materials. The U. S. Public Health Service and many local agencies investigating this problem have learned that the recommendations of the National Committee on Radiation Protection, although widely accepted by the medical and dental professions, are in many instances not being followed on a voluntary basis. Most nonradiologist physicians and dentists were found to be either unaware of the various Bureau of Standards handbooks in which the recommendations are published, or lacking in their understanding. In industry, there appears to have been a greater effort made to follow these recommendations, as well as those of the American Standards Association. Undoubtedly, union pressures, for justification of hazard pay, and industrial insurance efforts have been instrumental to that end.

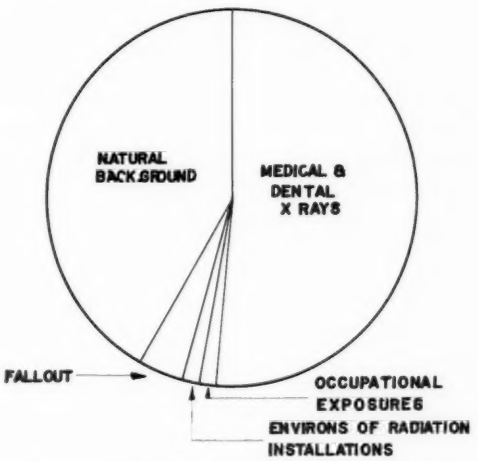

Fig. 1. Estimated gonadal radiation exposure Relative amounts of exposure from various sources for the average United States resident for the next few decades (barring nuclear war). (From recent Congressional Hearings on Fallout as quoted by Rogers McCullough, Chairman, Atomic Energy Commission Advisory Committee on Reactor Safeguards, Gatlinburg, Tenn., June 18, 1959.)

A provision of the Health Code requires that the Commissioner of Health approve all waste disposal activities within the city. In view of the large number of radiation installations registered (12,000), blanket approval has been given to all methods of waste disposal which have been listed by registrants on the registration form until such time as each method can be reviewed. This approach was taken because of the fact that by far the largest users of radioactive materials were under A.E.C. license and subject to A.E.C. inspection. The few unlicensed activities, such as radium dial-painting, are easily checked for improper practices.

The second part of the problem calls for

plans to guard against some of the adverse effects of radiation incidents and accidents. A careful review of all such occurrences in New York City, as well as in other parts of the country, indicates that, except for several accidents occuring at atomic energy research and development laboratories and plants, there have been few industrial radiation injuries. There has never been an actual injury as a result of radiation exposure in connection with a transportation accident or a fire. Although we do not discount the possibility of an injury or a hazardous spread of contamination under these circumstances, we consider an important part of this problem to be the public relations aspect of minor incidents. Because of confusion and uncertainty, the worst has been suspected, and in most cases scare headlines in local papers have resulted. We believe that the best approach to the solution of this problem is preparedness.

In the program of preparing for radiation accidents, the Board of Health amended the Health Code to include a section whereby the Commissioner of Health could publish a list of quantities and types of radioactive materials, which, if involved in an accident or fire, could constitute a public health hazard. In co-operation with the Atomic Energy Commission, a list of such items was drawn up and published. The Commission also co-operated to the extent of supplying a register of about 300 possible shippers of such materials. The section in the Code covering this matter requires that any shipper of such specified materials must notify the New York City Department of Health in advance of every such shipment, giving certain descriptive information about the contents, the method of shipment, route, and destination. The A.E.C., the Department of Defense, the U. S. Coast Guard, and the New York State Office of Atomic Development have been most co-operative in working out the mechanism for keeping track of such shipments. The New York City Police, Fire, and Traffic Departments have designated certain routes through the city, connecting with major air, rail, and ship terminals, which should be followed. The City reserves the right to limit the time of day during which such shipments may pass through particularly congested areas.

THE PROGRAM

On the basis of the pre-program study, early inspection of all installations was planned. Since, however, over 12,000 installations had been registered within the first few months of operation of the Code, it was decided that the initial inspection must be sharply limited in scope. This would, we believed, serve best to correct the most serious deficiencies in the shortest time. A few such deficiencies may be mentioned: It was observed that an alarming number of x-ray films were being taken without limitation of the useful beam to the area of clinical interest, as recommended by the N.C.R.P. In particular, many chest studies were being made under conditions in which the reproductive organs were exposed to the useful beam (see Fig. 2). This failure of collimation was also found in many dental installations, where large areas of the head were being exposed rather than the small part of the face necessary for a satisfactory radiograph. It was also observed that many x-ray technicians were not fully shielded by the protective barriers usually provided for the purpose. Technicians were quite commonly seen looking out from behind shields while making exposures, thereby subjecting their faces and chests to scattered radiation.

Many estimates have been made of the population dose both here and in England. Recently several groups have sampled x-ray examinations for large populations. Most such studies have assumed that, except in infants, the gonads are not usually exposed to the useful x-ray beam. Our preliminary inspections show this not to be true. If early findings are representative, estimates of population gonad dose from chest examinations will have to be revised upward. A chest film taken with a round

cone should show corners that have been cut off if a serious attempt has been made to limit the beam to the area of clinical interest, yet this is rarely true of the films usually exhibited.

On the other hand, some typical aspects which we considered of insufficient importance to include in the initial inspection are the possibility of excessive leakage from the tube head shield and the exact radiation output at a fluoroscopic panel. Except in extreme cases, the first cannot add significantly to the patient's integral dose and we rely on the assurance of the glass so that he can determine whether a fluoroscope is provided with lead glass approximately equal to his sample or, instead (as has been reported), with plate glass which has been substituted for broken lead glass. In addition, the screen is useful for checking dental beams. The inspector is also provided with a form on which he sketches a scale drawing of the arrangement of the room and equipment and indicates the nature and degree of all adjacent occupancy, including the spaces below and above.

In 1956 the National Academy of Sci-

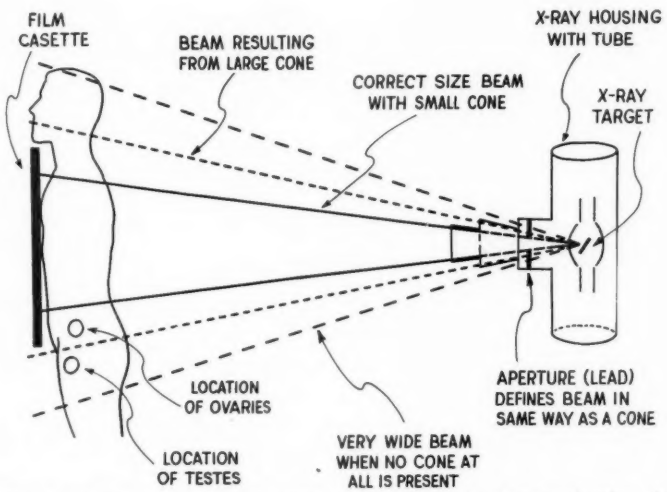

Fig. 2. X-ray collimation in chest radiography. A diagram showing the importance of the use of proper cones in reducing gonadal exposure.

various equipment manufacturers supplemented by spot checks of our own. In fluoroscopy, if the tube-to-panel distance and filtration are known, the output is predictable within reasonable limits for any particular technic. Doubtful cases are noted for follow-up measurements.

In order to correct the most serious deficiencies at an early date, it was decided to inspect x-ray installations in three stages. Stage 1 consists of visual inspection against a check list. The inspector is provided with a gauge for measuring filter thickness, a tape measure, and a piece of fluorescent screen with a sample of lead

ences recommended a sharp reduction in permissible exposure of the general public. This recommendation was accepted by the National Committee on Radiation Protection, which in a statement issued in January 1957 called for a thirty-fold reduction in maximum permissible radiation exposure to those in the environs of a radiation installation. The statement of the Committee (Jan. 8, 1957) reads, further: "Because of the impact of these changes and the time required to modify existing equipment and installations, it is recommended on the basis of present knowledge that a conversion period of not more

than five years from January 1957 be adopted within which time all necessary modifications should be completed."

We are particularly interested in the effect of this recommendation because 27 per cent of the installations in New York City have x-ray equipment over twenty years old. While there is no particular concern for the safety of such equipment, structural shielding installed over twenty years ago is not apt to meet the new standards. Sample measurements have been made in a number of offices located in residential and office buildings, and it is certain that many of the older installations will require augmented structural shielding. Although three years of the five-year recommended conversion period have already elapsed, we have not yet found a single instance where structural shielding has been modified to meet the new standards. In the case of 200-kv x-ray therapy installations, many of which were made in New York City during the 1930's, spot checks show that very few, if any, such installations included structural shielding in the ceiling. Shielding recommendations in *Handbook 60* indicate that a 200-kv x-ray unit operating under a moderate workload would require something on the order of 4 mm. of lead or 12 in. of concrete even if the ceiling height were 10 feet and the useful beam were never to be directed at the ceiling. In certain old buildings there is some question as to whether the structure could support so much weight safely. Owners of such installations will soon be advised that some thought should be given to the need for supplementary shielding in order to comply with our Health Code.

In the recommendations of the N.C.R.P., as well as those of the American College of Radiology and of the U. S. Public Health Service, the need for eye adaptation in fluoroscopy is frequently mentioned. Yet, it is often found that neither adequate room-darkening facilities nor, in many instances, the necessary red goggles are available. It is frequently admitted that no time is taken for eye adaptation. (It should be noted here that most of the fluoroscopes are in the hands of nonradiologists.)

In the case of x-ray therapy, it is believed that the most common cause of overexposure to a patient is error in filtration. Although there is no specific recommendation to cover this, there is a warning that "the filter system shall be so arranged to minimize the possibility of error." This has been interpreted, on the recommendation of the Advisory Committee, to require that the operator at all times be able to determine what filter is in place. Either an electrical indicating device is required or, as an alternative, filters may be provided with flags or colored ribbons to indicate when they are in position.

In the case of fluoroscopes, compliance with N.C.R.P. recommendations has been required without exception and has been considered to be most important because of the large contribution to the population dose estimated to be attributable to the use of fluoroscopy, particularly among nonradiologists.

The second stage of inspection consists of a further visit, if indicated, at which time a measurement of the fluoroscopic output is made if the kilovoltage, the milliamperage, the tube-to-panel distance, and filter could not be determined by inspection. In this second stage any particularly critical measurement is also made, as, for example, to determine whether there is adequate shielding behind a wall-mounted film-holder or under a table, where the areas beyond are occupied. Questionable lead glass is also checked.

The third stage is to be a general test of structural shielding where shielding is needed. It is planned to accomplish this by the use of a radioactive source and to supplement such measurements with test films to be posted at important locations and left for a period of several weeks.

EDUCATION

No radiation control effort would be complete without a professional and public educational program. We have supplied

each physician and dentist with a copy of *Handbook 60*. In addition, bulletins of information have been prepared, abstracting the most important rules for each type of equipment, including medical radiographic, dental, mobile, therapy, and fluoroscopic. Two meetings have been held with x-ray manufacturers and dealers to explain their responsibilities which are specified in the Code. Professional societies have been addressed and we have established a technical reference library. The increasing number of questions and requests for assistance indicates progress. We have available for registrants a list of approved radiological physicists and film-badge services. An exhibit is being constructed for showing at appropriate places.

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SUMMARIO IN INTERLINGUA

Un Comprehensive Programma pro le Controlo del Radiation in le Citate New York

Le Codice de Radiation pro le Citate New York, in fortia depost le 15 de junio 1958, require le registration de omne fontes de radiation intra le citate e require le observation del recommendationes del Committee National pro le Protection Contra le Radiation.

Le programma pro le controlo del radiation ha duo aspectos: (1) Le administration del Codice Sanitari visante a assecurar que technicos de radiation, patientes medical e dental, e le population general non es exponite routinarimente a evitabile formas de radiation e materia radioactive e (2) le protection contra certes del effectos adverse de incidentes e accidentes de radiation.

Es facite tres inspectiones de omne registrate installationes. Al tempore de su prime visita le inspector tenta corriger le plus serie violationes, per exemplo le non-restriction del utile fasce diagnostic al area de interesse, le non-provision de un efficace armatura pro le technicos, e le incorrecte uso de vitro blanc in loco de vitro a plumbo in fluoroscopios. In le caso de fluoroscopios, obedientia immediate al regulationes del codice es requirite. Isto es considerate como importante a causa del grande contribution facite per fluoroscopios al dose de radiation recipite per le population, particularmente inter non-radiologos.

Le secunde stadio del inspection consiste de un secunde visita que se occupa—si indicate—de mesurar le rendimento fluoroscopic, in caso que le kilovoltage, le milliamperage, le distantia inter tubo e pannello, e le filtration non poteva esser determinate al tempore del prime visita, e de effectuar altere mesurationes que es particularmente critic.

Le tertie stadio, non ancora executate al tempore del presente reporto, consiste de un examine general del protection structural in tanto que isto es requirite.

A parte le supra-citate mesuras, un extense programma de education professional e public ha essite initiate. Isto include le distribution a omne medico e a omne dentista de exemplares del *Handbook 60* (= *Manual 60*) e de bulletins e summarios de information, le organisation de conferentias con fabricantes e venditores de apparatos de radiation, le presentation de discursos a societates professional, e le establimento de un bibliotheca de consultation in le campo del technica radiatori.

The Use of Photocells for Determination of Patient Movement During Roentgen Therapy*

BERNARD ROSWIT, M.D., STANLEY J. MALSKY, M.A., M.Sc., CYPRIAN REID, B.Sc., and CHARLES SPRECKELS

IN ROENTGEN therapy, it is imperative that the anatomical part harboring the lesion be completely immobilized during exposure to the beam. Particularly is this so in radical therapy of radiocurable cancer. A method for maintaining a graphic record of the patient's movements, if any, and for continuous surveillance during x-ray therapy would be most desirable. The reliability of immobilization technics,

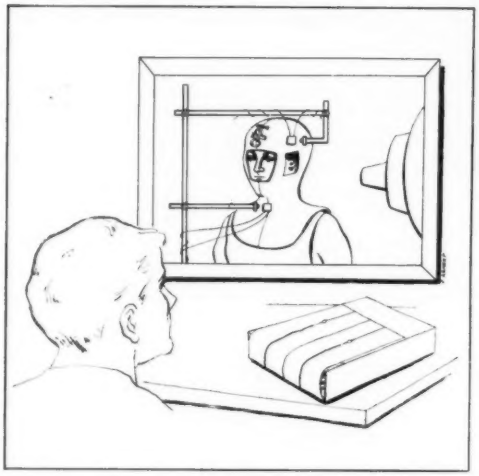

Fig. 1. Drawing of photocell system in clinical practice for determination of patient movement during roentgen therapy.

the accuracy of beam direction, and the patient's co-operation may thus be permanently recorded and carefully evaluated. We have designed and adopted a simple, effective, and relatively inexpensive system for this purpose, utilizing a miniature photocell, a light pipe, and a graphic recorder (Fig. 1).

Miniature photocells are mounted on a plaster bandage treatment shell on the patient's body at any two selected points at

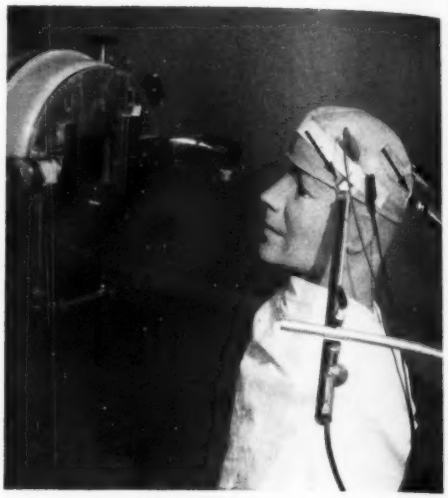

Fig. 2. Photocell system mounted on phantom.

90° to each other (Fig. 2). A light source is placed in close proximity to each photocell.

Dual strip chart recorders are employed to plot the slightest displacement of the two selected reference points. Any variation from a straight line on any chart indicates the degree of change in the patient's position in one axis or another, or in both, during the period of irradiation. If one desires only to monitor the patient's movements, the use of a simple milliammeter instead of a recorder will prove adequate. The component parts of the assembly for the illuminating photocell are illustrated in Figure 3.

Prior to the final selection of the photocell for use in our system, we investigated a large variety of such units (see Table I). The following factors were considered in our study: (1) size of sensitive area, (2) stabilization of reading under x-radiation, (3) meter displacement (microamperes) vs.

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[1] From the Radiotherapy Service, Bronx Veterans Administration Hospital, New York, N. Y. Accepted for publication in May 1959.

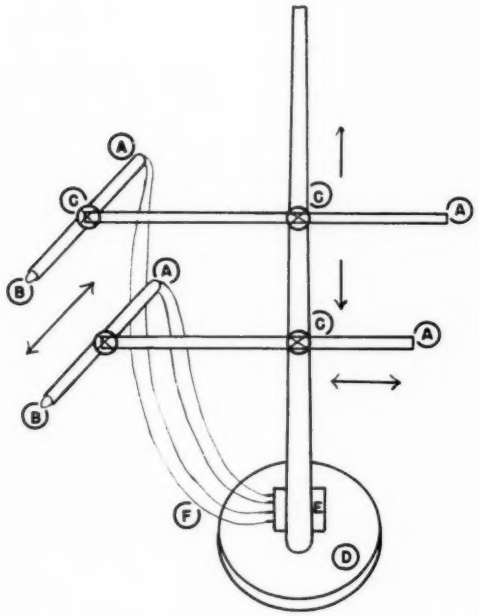

Fig. 3. Schematic drawing of completed photocell system indicating essential components in relative positions. A. Hollow aluminum tubing. B. Pilot light assembly (6 volts D.C.). C. Locking unit so that vertical and horizontal bars can be adjusted for individual patients. D. Base support, iron and lead filled. E. Electrical connections that pass through the short aluminum arms of A and are attached to the pilot light assembly.

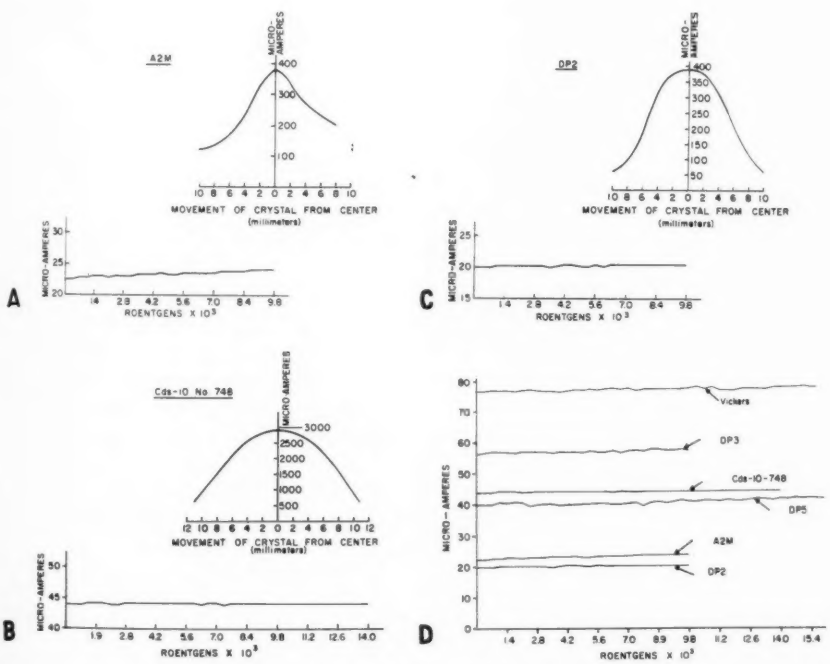

Fig. 4. Charts illustrating the radiation effect upon each crystal, as well as displacement of the crystal with respect to the fixed light source.

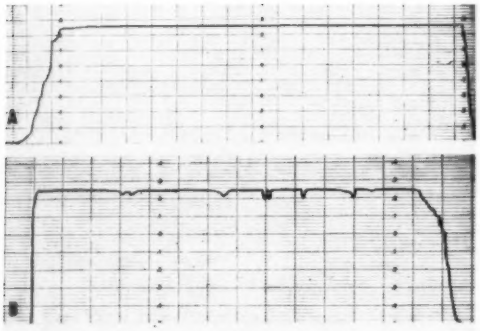

Fig. 5. A. Normal curve. B. Periodic coughing. C. Crystal displacement 1/2 inch and 1/4 inch from center of light source.

movement, and (4) facility of crystal mounting.

Each of the photocells was first subjected to a total dose of approximately 10,000 r for a study of the effects of primary and scattered radiation on the light-current output. Variations or fluctuations, if induced by ionizing radiation, would render a monitoring system unreliable. The results are recorded in Figure 4, A, B, and C, showing the current in microamperes *vs.* irradiation effect upon each crystal.

In addition, displacement of the crystal with respect to the fixed light source is also included (microamperes *vs.* movement of crystal). The fall-off of current as a function of cell movement per millimeter is quite appreciable and can easily be discerned. In Figure 4, D, a graph showing the fluctuations of the various photocells is reproduced. From among these, Cds-10 cell was finally selected for our use.

Figure 5 presents tracings made under three conditions during treatment in our

TABLE I: PHOTOCELLS INVESTIGATED

	Photocell Type*	Dimensions	Power Source
A	B-2M	23/32″ × 7/16″	None
	B-15	1 11/16″ × 1 11/16″	Battery, resistor
	DP-5	1 11/16″ × 1 11/16″	Battery, resistor
	AZM	9/32″ dia.	Battery
	DP-3	9/16″ × 3/8″	Battery, resistor
	DP-2	15/32″ × 3/16″	Battery
B	CL-1	5/32″ dia.	None
C	Mounted	1 5/8″ dia.	Battery, resistor
D	Cds-10	1/2″ × 3/8″	Battery

* CL-1, Clairex. Mounted, Vickers. Cds-10, Hupp. All others, International Rectifier Corp.

Radiation Clinic: The curve labeled A indicates the pattern to be expected with no movement; B shows the effect of periodic coughing; C records the movement of the patient's head, which was repositioned and again moved. It further indicates that cranial displacements as little as 1/2 or 1/4 inch produce a striking change in the recorded tracing.

Two cells are always employed, mounted, as stated above, at 90° with respect to each other, on the patient. In our experience, plaster treatment shells have become an indispensable adjunct to precisional roentgen therapy, especially in the treatment of cancer of the head and neck.

SUMMARY AND CONCLUSIONS

1. In roentgen therapy it is mandatory that movement of the patient during exposure be completely restricted.

2. A system is described for continuous surveillance and graphic recording of the patient's movements during the treatment period. This involves the use of miniature photocells, mounted on a plaster treatment shell, a light pipe, and recorder assembly.

3. In actual practice the system has proved to be fairly simple, relatively inexpensive, and entirely reliable.

NOTE: We express our appreciation to Mr. E. Kerut, our Mechanical Engineer, and Mr. L. Maddalone, our Mold Technologist, for their assistance.

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(*Pro le summario in interlingua, vider le pagina 484*)

Device for Registering Depth of Cut in Polycassette Tomography[1]

CLARENCE B. HORTENSTINE, M.D.[2]

BODY-SECTION roentgenography, especially of the chest, is extensively utilized in the McGuire Veterans Administration Hospital. The use of a seven-film polycassette with a single sweep of the tube has served to reduce significantly the total amount of radiation necessary to obtain a satisfactory examination. This procedure, however, presented difficulties in efficiently labeling the separate films for identification. Some system was called for, by means of which each film could be permanently marked with its correct depth level.

The simple, easily handled device depicted in Figure 1 is an original design of the author and was constructed by him from easily obtainable materials.[3] It consists of 1/4-inch lead numbers placed 90° apart in spiral staircase fashion about a small plastic central rod, with a vertical distance of 1.0 cm. separating each number from that preceding and succeeding it. The central rod with numbers attached is placed within the lumen of a plastic tube having an inside diameter of 1 inch, both tube and enclosed rod being cemented with plastic glue to a small base. The top of the tube is closed with another small plastic disk. The device is so constructed that the lowest number corresponds to the exact distance in centimeters from the table surface of the base, and thus also from the body surface in contact with the table top. The example pictured covers levels from 4 through 18 cm., but the levels can be varied to fit the particular need.

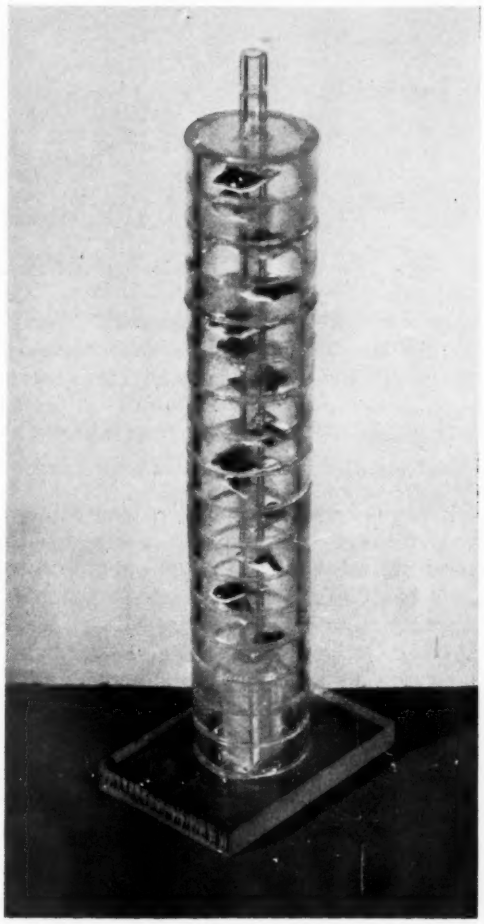

Fig. 1. Device for registering depth of cut in polycassette tomography.

In operation, the device is placed beside the patient during exposure, and the number most clearly registered on each film corresponds to the actual depth of cut at that particular level, as all numbers above or below the level registered are wiped out or appear only as blurs. Each film in the polycassette is thus imprinted at time of exposure with its particular depth of cut.

[1] Accepted for publication in April 1959.

[2] Resident in Radiology, McGuire Veterans Administration Hospital, Richmond 19, Va.

[3] The author expresses his appreciation to Mr. Merlin S. Snowden, Medical Equipment Repairman, and to Mr. Robert H. Patton, Chief Medical Radiology Technician, for their suggestions and assistance in fabricating and testing this device.

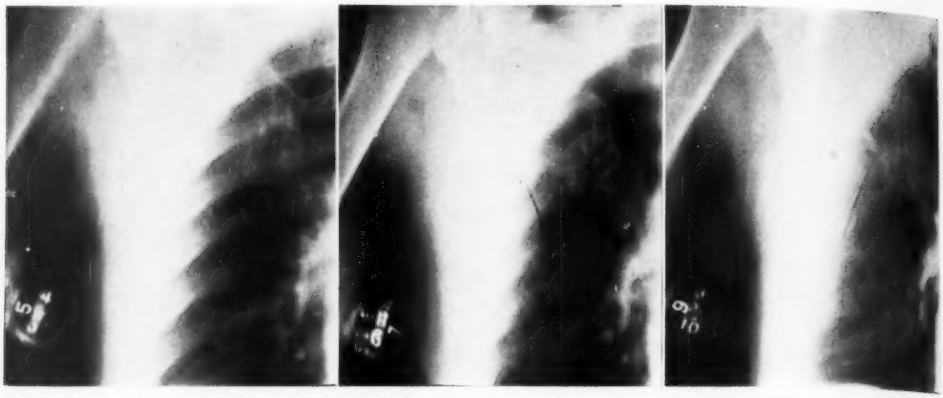

Fig. 2. Cuts at 5-cm., 7-cm., and 9-cm. levels obtained with a polycassette, with a single sweep of the tube, showing the depth of the cut registered on the film. The 9-cm. cut shows that 9.2 cm. is the more exact level.

This accomplishes a considerable saving in time and also serves to abolish possibility of error, as formerly all films were placed in their proper level by inspection and the depth of cut was marked on each by hand.

SUMMARIO IN INTERLINGUA

Dispositivo pro Determinar le Profundor del Sectiones in Tomographia Polycassettal

Es describite un dispositivo pro marcar le successive sectiones in tomographia polycassettal. Numeros de plumbo es placiate spiralmente a intervallos de 90 grados circum un micre virga de plastico con distantias vertical de 1 cm. Le virga con le numeros es includite in un tubo de plastico, e isto es placiate juxta le patiente durante le exposition. Le numero que es inscribite le plus clarmente in le pelliculas individual corresponde al ver profundor del section.

SUMMARIO IN INTERLINGUA

Le Uso de Photocellulas pro Determinar le Movimento del Patiente Durante le Therapia Roentgenologic

(*Pagina 480*)

In le roentgenotherapia il es necessari restringer completemente le movimento del patiente durante le exposition. Es describite un systema pro le continue observation e le registration graphic del movimentos del patiente durante le periodo del tractamento. Le apparatura consiste de micre photocellulas (montate super un modulo de gypso que se applica al corpore del patiente), un fonte de illumination, e un mechanismo registratori.

In le practica le systema se ha provate satis simple, relativemente incostose, e completemente fidel.

EDITORIAL

The Future of Radiology[1]

Anyone who attempts to visualize the developments of the future or tries to prophesy what changes may take place is in an extremely ticklish position. Having no crystal ball, I have no uncanny premonition of what lies ahead; no magic wand to wave to prevent or change or cure. I intend, however, to touch mainly on three ways by which Radiology may be affected in the next ten years.

"Health in its broadest aspects has importance to our nation second only to our national security." To this statement in *The Challenge to America: Its Economic and Social Aspects* (1), many of us might take exception, placing health first rather than second in importance, since without health national security can only fail. This report brings out possible developments in medical care for the future and emphasizes the importance of research and the fact that all medical groups should participate therein and impart their information to the public. Radiology, solidly ensconced as the practice of medicine, cuts across all of Medicine and Surgery more than any other specialty. What happens in this field, therefore, whether it be in relation to research, methods of practice, or education, is very likely to happen to all other branches of Medicine.

The following opinions, and mere opinions are what they are, have been formed from certain observable trends and inferences drawn therefrom. They deal with education, research, and methods of practice.

EDUCATION

It goes without saying that education shapes the future of Radiology. This applies not only to our own education as we attend this or similar meetings, but even more significantly to those who are to be trained in the specialty. The responsibility lies with the teacher as to the man he selects, how well the material is presented, and how well the student may be stimulated to self-education and investigation. Although there is much to be said concerning undergraduate training, this aspect will not be emphasized, as other points are probably of more immediate concern to us today, particularly resident training and how it may be improved.

Current newspaper articles indicate the public interest in undergraduate medical education and frequently point out that there is a considerable decrease in the number of applicants to medical schools. The disturbing element, however, is not only in the lessening of the quantity but in the lowered quality (the intellectual ability) of the individual applicant. It will doubtless remain true that a certain percentage of high-grade persons will enter the field of Medicine, but unfortunately a much larger number appear to be electing other scientific fields (2). Should this continue to a point where the applicants as a group are of such low aptitude as to be incapable of making progress in the treatment of disease, there will be cause for real alarm, not only for Medicine but especially for Radiology. There is a lessening tendency in medical schools to stress the teaching of Radiology as a specialty, its application falling into other branches of the curriculum. Fortunately those in closer touch with the undergraduate area are utilizing new ideas, with rearrangement and revision of courses as well as shortening of the time

[1] Presidential Address delivered before the Radiological Society of North America at its Forty-fifth Annual Meeting, Chicago, Ill., Nov. 16, 1959.

requirements. It is hoped that their efforts will tempt the best grade of candidates to return to Medicine.

Resident Training: In this period of transition, where there are vast amounts of new information available, certain trends in methods of teaching may be worth considering and possibly applying to Radiology. One of these is the so-called unit system (3). The outstanding merit of this system is that each subdivision of a specialty has a man at its head who is primarily a fundamental investigator and secondarily an experienced clinician. It is imperative that a definite balance between clinical activity and research be maintained, so that the patient as a whole is understood and properly treated. Each unit is well integrated and is set up in somewhat the same plan as the entire department. As applied to Radiology, the various units could be in the field of diagnosis, therapy, physics, isotopes, radiobiology, and research. Let it be emphasized that intercommunication must be extremely active and constant.

In all specialties the effect of the various certifying Boards on the field of graduate education has been noted and has been the source of polemic discussions. Whatever the extent of controversy may be, it must be recognized that a Board exerts a certain directional influence on its particular specialty. Because of this influence, certain responsibilities clearly fall on the Board. The thinking should be decisive and directed toward the best education of the candidate. It is my own contention that a training program in Radiology should make every effort to surpass all of the requirements of the American Board of Radiology but, without ubiquitous assistance, blind spots in training programs can develop and grow.

Some would accuse the American Board of Radiology of heterophemia, but it should be recognized that a period of transition is going on. A certain amount of unrest and possibly misunderstanding as regards some of the requirements have resulted. Where is the training concerning isotopes to find its leveling off? Where is the emphasis on physics and radiobiology going? What types of examination should be carried out? These are some of the problems pointed out by Donald S. Childs (4). The present status is fluid and by no means final.

A re-evaluation and re-inspection of approved residency programs has recently been undertaken. Within the next few months the criteria for approval of various teaching institutions must be considered and faced squarely. The final decisions will be determined from the studies of the American Board of Radiology and the Residency Review Committee, through the Council on Medical Education of the American Medical Association.

Returning for a moment to the number of persons entering the field of Medicine, it is worth noting that there are many unfilled approved residencies. It may be that the decrease in the number of students going into the field of Medicine has been reflected much more strongly in Radiology than in other specialties. Although the greatest depletion has occurred in the small institutions or those which are not related to a university teaching program, even some of the large departments are having difficulty in finding highly qualified persons to fill their openings.

If a program is to be approved, it must offer a broad coverage in diagnosis and adequate training facilities for all forms of x-ray therapy. There must be ample and active participation in radium therapy. Isotopes should be included both in diagnosis and in therapy. Physics teaching has to be active and there is also a demand for inclusion of radiobiology. Beyond this there may well be the requirement for research programs, particularly in those institutions training men for the academic positions of the future. And in these research programs not only physics but most of the basic sciences will need to be represented.

May the ultimate decisions affecting education be wisely and judiciously made. Let it be reiterated that education is one of

our most vital building blocks for the future of Radiology.

RESEARCH

The need and opportunity for research face all branches of Medicine today. Radiologists are said to have been lax in seizing opportunities, although applied research, the development of ideas, and clinical research have been done well by many radiologists over the years. Basic research, investigation merely for information or understanding of a subject, however, has received relatively little attention. An anamnestic analysis might indicate that serendipity may have been a determining factor in our acquisition of knowledge.

Possibly one of the best modes of improving public relations would be to show that we are looking to the future and are doing a significant share in the field of basic research. This could well be of value not only in destroying outmoded ideas but finding new information which might or might not be applied in the clinical field. A recent book entitled *Symposium on Basic Research* (6) contains a large number of papers concerning this subject. To those interested, it furnishes a base line from which to do constructive thinking. Important requirements are the obtaining of proper personnel, provision of the right working environment, and stimulation of the individual to make time for free, uninterrupted thinking without demands for immediate or applicable answers—to satisfy a personal thirst.

What can be done in the field of research? As yet we have no definite answer concerning the interaction of radiation and matter, although some attempts have been made in this direction. It could be that part of the problem has been the lack of interest on the part of thoroughly trained radiologists in the field. Had they applied their wide fund of information to such a search, we might now be considerably wiser. Many of those who have done basic investigation in radiobiology have been outside the field of Radiology. Radiology should not have a monopoly over radiobiology or radiophysics but, by the nature of our training, we should be fitted to assist the radiobiologist or the radiophysicist in his search for basic information.

Radiologic physics has much to do in the field of improved technics of diagnosis, dosimetry, and perhaps some of the automation methods, such as electronic taping, storage tubes, and other applications of television principles, as well as utilization of some of the circuitry and instrumentation used in missile and space rockets. This is actually applied research that might be readily adapted to the clinical field.

In radiation therapy there are many studies that could go on with high-energy radiation, such as gamma radiation from Cobalt 60, the Van de Graaff type of generator, and linear accelerators. High-energy particles such as deuterons and protons from cyclotrons and the synchrocyclotrons are also worthy of diversified study. In basic investigation there remains much to be done concerning desoxyribonucleic acid (DNA), cell cultures, and the analysis of values of potentiators such as oxygen or some of the protein synthesis inhibitors. A better understanding and knowledge of why or how these agents may participate is badly needed. Application of the information obtained might well follow, but primarily information is required.

One word of warning, however: Do not *swamp* the true researcher in the administration of such programs. It is imperative that the person who is interested in investigation should not become worn down with managing contracts, projects, guiding assistants, and writing out project plans. When one studies the amount of submitted material and reports necessary to carry out a research project, one can foresee the possibility of the submergence of a person capable and educated for research in the morass of unessential minutiae (8).

Radiology should implement basic investigation in which conformity has to be abolished, originality has to be fostered,

and responsibility has to be accepted (9). Some of us "old-timers," whether we like it or not, must hereafter think more in the way of fundamental investigation. The time has come to seek sources to provide support for free thought and investigation without direction, restriction, or compulsion.

METHODS OF PRACTICE

In the future, methods of practice of Radiology may well be those which are applied to other divisions of Medicine. Its practice now and heretofore has caused much controversy among educators, clinicians, and administrators. Possibly some of the ill feeling that has arisen has resulted from misunderstanding. Nevertheless, there are certain trends in methods of practice which may continue and which could develop into very undesirable situations before any realization of their pending accomplishment occurred. These the radiologist should try to understand and be prepared to meet and guide.

Is there a place in the future for the practice of Radiology as a specialty? A study of Galdston's article "The Birth and Death of Specialties" (10) reveals that certain specialties have developed because of the need to study the etiology, diagnosis, and treatment of a specific disease; as various diseases are conquered, we can understand why some specialties are disappearing. Galdston also stresses that certain specialties are born and grow because of the utilization of a specific instrumentality. Radiology is based upon the use of a specific agent and because of the method of application peculiar to it, it should continue well into the future.

How may the specialty be practiced to greatest advantage to the patient? Elsewhere the unit system as applied to teaching has been discussed. Extension of such a system to the actual practice of Radiology is possible. I see no reason why the person who wishes to spend the greater portion of his time, or all of his time, in any particular branch of Radiology should not do so. However, separation from the specialty, and the decision that any one particular division is equal to the whole, could well result in a serious detriment to the patient, Medicine, and Radiology. Synecdochism is inappropriate, and the common specific agent should be the common denominator of preserving unity.

With the rapid advances in Medicine, it has been recognized for a long time that no one individual can know all of medicine, and there is question also whether any one individual can know all of one specialty. As a result, there has been a growing increase in the practice of physicians in groups and clinics. Now there seems to be an equally strong trend toward the development of practice within hospital confines. The Rorem Report (11) in a brief summary makes it increasingly apparent that the trend is progressing. In all likelihood the next step will be abolishing of differentiation of the private from the ward patient. Practice in hospital groups may result in all patients being seen in similar environs no matter what their socioeconomic status. It is further pointed out that the day of the fee for service type of practice may be fast disappearing (12).

Other portents to be heeded include the possibility of complete submergence of the practice of Radiology into institutions. Even today, if one studies the effect of voluntary health insurance, it is seen there is a constant pressure to force it into the hospitals as a technical service. This, along with the growth of practice of all forms of medicine in hospitals, makes it easy to envision the relative facility with which government medicine could become a reality. Perhaps an initial step in that direction came with the introduction of Medicare. The full implications of the Forand bill could accelerate these processes.

At the time that the British physicians came under the National Health Service, the late Merrill C. Sosman said to me: "It takes about fifteen years for this country to follow the footsteps of England." Perhaps his prediction may prove to have been accurate. Although it is difficult for

nonperegrinating radiologists to understand what is going on in England, the *New England Journal of Medicine's* "By the London Post" (14) could give some idea of the possible problems. British physicians have been harassed with much discomposure, which has resulted in an exodus to a point that could become alarming. Financial problems of the physicians are least important, but lack of hospital beds and of adequate equipment and resultant delays in care of patients are most distressing. This confinement, regulation, and restriction imposed on the way of a British physician's practice could apply to us in the future. Should this appear imminent, we must be in a position to guide principles of practice so that we may evolve a superior way of taking care of our patients. I for one sincerely hope that it will be possible to refine the methods of private enterprize (in contrast to socialization or nationalization) so that patients may have the ultimate in medical care at reasonable, prepaid, and all-inclusive rates without having the medical profession subjected to the controls and difficulties which usually occur under Government regulation.

In closing, I am firmly optimistic about the future of Radiology. It will require careful preparation for change: constant study, revision and application of attitudes in the education of the student (and ourselves); unrelenting search for new and real opportunities for basic research; and judicious direction of evolving methods of practice to provide the best care of the patient. LAURENCE L. ROBBINS, M.D.

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ANNOUNCEMENTS AND BOOK REVIEWS

AMERICAN BOARD OF RADIOLOGY

The Spring 1960 examination by the American Board of Radiology will be held at the Terrace Hilton Hotel, Cincinnati, Ohio, June 6–10. The deadline for filing applications was Jan. 1, 1960.

The Fall 1960 examination will also be held in Cincinnati, Dec. 5–9. The deadline for filing applications is July 1, 1960. A Special Examination in Nuclear Medicine for those diplomates in Radiology or Therapeutic Radiology will be offered, provided there are sufficient applications.

H. DABNEY KERR, M.D., *Secretary*

BROOKLYN RADIOLOGICAL SOCIETY

Newly elected officers of the Brooklyn Radiological Society are: President, Solomon Schwartz, M.D.; Vice-President, George A. Manfredonia, M.D.; Secretary-Treasurer, Isadore Katz, M.D., 450 Clarkson Ave., Brooklyn 3, N. Y.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY

New officers of the Central New York Radiological Society are: Robert J. MacCallum, M.D., Utica, President; E. Robert Heitzman, Jr., M.D., Syracuse, Vice-President; Joseph A. Head, M.D., Hospital of the Good Shepherd, Syracuse, Secretary-Treasurer.

GREATER MIAMI RADIOLOGICAL SOCIETY

The Greater Miami Radiological Society has elected the following officers for the coming year: President, Andre S. Capi, M.D., Hollywood; Vice-President, George P. Daurelle, M.D., Miami; Secretary-Treasurer, Donald H. Altman, M.D., 2751 Coral Way, Miami.

SAN FRANCISCO RADIOLOGICAL SOCIETY

The San Francisco Radiological Society has recently elected the following officers: John F. Huffman, M.D., President; Martha E. Mottram, M.D., President-Elect; Merrell A. Sisson, M.D., 450 Sutter St., San Francisco 8, Secretary-Treasurer; James T. English, M.D. and John R. Bryan, M.D., Members of Executive Board.

CENTRAL AMERICA AND PANAMA RADIOLOGICAL SOCIETY

At its recent annual meeting, the Central America and Panama Radiological Society (Asociación de Radiólogos de Centro America y Panamá) elected as Secretary-General, Dr. Julio Toriello de Leon, 11 Calle 2–37, zona 1, Guatemala, C. A., and as Vice-Secretary, Dr. Roberto Calderón of Nicaragua.

CANADIAN ASSOCIATION OF RADIOLOGISTS

The Twenty-third Annual Meeting of the Canadian Association of Radiologists held at the Royal York Hotel, Toronto, Ont., Jan. 24-27, 1960, was attended by some 200 doctors from across the Dominion. The scientific highlight of the meeting was the Gordon Richards Memorial Lecture, given by Robert S. Stone, M.D., Professor of Radiology, University of California School of Medicine, San Francisco.

EASTERN RADIOLOGICAL CONFERENCE

The Eastern Radiological Conference, sponsored by the New England Roentgen Ray Society, will meet at the Sheraton Plaza Hotel, in Boston, Mass., April 21–23, 1960.

The scientific program, beginning on Friday, April 22, and closing at noon on Saturday, will feature symposia from the Harvard Medical School, the Peter Bent Brigham Hospital, the Massachusetts General Hospital, and the Massachusetts Institute of Technology.

Tours are being arranged to the Massachusetts Institute of Technology nuclear reactor, to the 6-billion-volt Cambridge accelerator, to the High Voltage Engineering Company, and to the AVCO Research and Advanced Development plant.

The registration fee of $30.00 covers the cost of the annual banquet, a reception on April 21, and the tours. There will be a fee of $20.00 for wives participating in the ladies' program.

Further information may be obtained from John E. Gary, M.D., Secretary, The New England Roentgen Ray Society, 1180 Beacon St., Brookline, Mass.

UNIVERSITY OF ROCHESTER THIRD CINEFLUOROGRAPHY SYMPOSIUM

Plans are under way for the Third Symposium on Cinefluorography to be held at the University of Rochester School of Medicine and Dentistry in the Spring of 1961. Further announcements concerning meeting dates and program content will be published later. No meeting on cinefluorography is planned for the Fall of 1960.

SYMPOSIUM ON RADIOACTIVITY

The Section on Medical Sciences of the American Association for the Advancement of Science is

sponsoring a Symposium on Radioactivity in Man: Measurements and Effects of Internal Gamma-Ray Emitting Radioisotopes, to be held at Vanderbilt University, Nashville, Tenn., April 18-19, 1960.

The Conference was made possible by a grant from the United States Steel Foundation to the American Association for the Advancement of Science and is supported in part by the Division of Biology and Medicine of the Atomic Energy Commission, the Public Health Service, and the Army Medical Research and Development Command.

An excellent program has been prepared under the direction of the Symposium Chairman, George R. Meneely, M.D., School of Medicine, Vanderbilt University, Nashville 5, Tenn.

PAN-AMERICAN MEDICAL ASSOCIATION THIRTY-FIFTH CONGRESS

Among the fifty sections to be included in the Thirty-Fifth Congress of the Pan-American Medical Association meeting in Mexico City, May 2–11, 1960, will be those on Diagnostic Roentgenology and Radiation Therapy, under the direction of Eugene P. Pendergrass, M.D., Philadelphia, and Juan A. del Regato, M.D., Colorado Springs, Colo., respectively. Both Dr. Pendergrass and Dr. Regato are anxious for a highly representative participation in these sections.

For further information, address Philip J. Hodes, M.D., Department of Radiology, Jefferson Medical College Hospital, Philadelphia 7, Penna.

RADIOLOGICAL PHYSICS COURSE MEMORIAL CENTER, NEW YORK

The Department of Biophysics of the Sloan-Kettering Institute of Cornell University Medical College is calling to the attention of those interested its graduate student program in radiological physics. The curriculum includes formal courses in physics, biology, physiology, chemistry, and radiation physics. Extensive laboratory training in treatment planning, implant dosimetry, application of radioactive isotopes, measurement and calibration of isotopes and other radiation sources, and radiation protection is offered. A thesis is required for the M.S. degree. A limited number of fellowships are available.

Requests for information should be addressed to the Department of Biophysics, Sloan-Kettering Institute, Memorial Center, 444 East 68th St., New York 21, N. Y.

NEURORADIOLOGY COURSE COLUMBIA UNIVERSITY, NEW YORK

The College of Physicians and Surgeons of Columbia University is offering for the second year a course in Neuroradiology. This will be given by Juan M. Taveras, M.D., and his associates, April 11-15, 1960. The fee for the course is $100.00.

Application forms may be secured from Melvin D. Yahr, M.D., College of Physicians and Surgeons, 630 W. 168th St., New York 32, N.Y.

FELLOWSHIP IN NEURORADIOLOGY COLUMBIA UNIVERSITY, NEW YORK

The Department of Radiology at Columbia University-Presbyterian Medical Center, in cooperation with the National Institute of Neurological Diseases and Blindness, offers a two-year Fellowship in Neuroradiology at the Neurological Institute. The candidates must be radiologists who have completed their three-year residency training. The stipend is to be determined by the individual needs of the applicant.

Further information may be obtained from Juan M. Taveras, M.D., Columbia-Presbyterian Medical Center, New York 32, N. Y.

NEURORADIOLOGY GRADUATE TRAINING ALBERT EINSTEIN COLLEGE OF MEDICINE, NEW YORK

A two-year graduate training program in Neuroradiology, with support from the U. S. Public Health Service, will be available at the Albert Einstein College of Medicine in New York commencing July 1, 1960, under the direction of Dr. Mannie Schechter. This program, with emphasis on the correlation of neuroradiology with neuroanatomy, neuropathology, neurology, and neurological surgery, is open to physicians who have completed or are soon to complete a residency in Radiology.

FREEDMAN LECTURES UNIVERSITY OF CINCINNATI

On Saturday and Sunday, April 9 and 10, 1960, Dr. John W. Hope, Director of the Department of Radiology, Children's Hospital of Philadelphia, will deliver the 12th Annual Joseph and Samuel Freedman Lectures in Diagnostic Radiology at the University of Cincinnati College of Medicine. Physicians desiring to attend are requested to write Dr. Benjamin Felson, X-Ray Department, Cincinnati General Hospital, for further details. There will be no charge for the lectures.

HOSPITAL PHYSICISTS' ASSOCIATION

The Hospital Physicists' Association of Great Britain is calling to the attention of radiotherapists and radiation physicists its program for the interchange of data on radiation physics.

The Diagrams and Data Scheme of the Association was established in 1944 for the express purpose of collecting useful items of data on radiation physics from hospital physics departments and making these available generally. Since that time

many more hospital physics departments have been established and consequently there is now a larger amount of physical information available. At present many radiotherapy departments are adding high-voltage machines to their equipment and at the same time seeking reliable physical data in the form of curves and isodose distributions.

The Scientific Sub-Committee of the Association recently surveyed the data in the Scheme. Because a great deal of the material was considered obsolete and replaceable by more recent material, a new catalogue has been compiled, listing the presently available information and the sources of origin. Details of the method of ordering items of data are given in the catalogue and any material will be supplied providing it is not to be sold or reproduced for publication. The Scheme is non-profit-making and items are sold at the minimum price necessary to cover the running costs.

Copies of the catalogue may be purchased by anyone interested. For further information address the Hon. Secretary, Diagrams and Data Scheme, Physics Department, Mount Vernon Hospital, Northwood, Middlesex, England.

RADIOLOGY IN WORLD WAR II

Dr. Kenneth D. A. Allen, who is editing the History of Radiology in World War II for the U. S. Army Medical Service, is appealing to radiologists to assist in obtaining material for this work. He and his fellow editors are especially anxious to have as complete a list as possible of American radiologists who received citations or decorations from either the American Services or foreign countries (including honorary membership in foreign societies), in recognition of their services. He asks any such to lay aside personal modesty and report their honors. Any radiologists who know of enlisted personnel in their departments who received decorations or commendations are requested to report these also. Address Kenneth D. A. Allen, M.D., Editor, History of Radiology in World War II, 800 Washington St., Denver 3, Colo.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

SAFE HANDLING OF RADIOACTIVE ISOTOPES IN MEDICAL PRACTICE. By EDITH H. QUIMBY, Sc.D., Professor of Radiology (Physics), College of Physicians and Surgeons, Columbia University, New York, N. Y. A monograph of 130 pages, with 17 figures. Published by The Macmillan Company, New York, 1960. Price $4.50.

ISOTOPIC TRACERS: A THEORETICAL AND PRACTICAL MANUAL FOR BIOLOGICAL STUDENTS AND RESEARCH WORKERS. By G. E. FRANCIS, Reader in Biochemistry, St. Bartholomew's Hospital Medical College, W. MULLIGAN, Senior Lecturer in Biochemistry, Glasgow University Veterinary School, AND A. WORMALL, Professor of Biochemistry, St. Bartholomew's Hospital Medical College. With a foreword by G. Hevesy. A volume of 524 pages, with numerous figures and tables. Published by University of London, The Athlone Press, 2d ed., 1959; Oxford University Press, New York, 1960. Price $8.40.

ROENTGEN EXAMINATIONS IN ACUTE ABDOMINAL DISEASES. By J. FRIMANN-DAHL, M.D., Ph.D., Chief of Roentgen Department, Ullevål Hospital, Oslo, Norway. A volume of 518 pages, with 446 figures. Published by Charles C Thomas, Springfield, Ill., 2d ed., 1960. Price $15.50.

THE DEVELOPMENT AND THE EMBRYONIC ANATOMY OF THE HUMAN GASTRO-INTESTINAL TRACT: A NEW BASIS FOR THE STUDY OF ANOMALIES OF THE GASTRO-INTESTINAL TRACT. By NIELS LAUGE-HANSEN, Medical Dr., R., Chief Radiologist, Central Hospital, Randers, Denmark. A volume of 86 pages, with 176 figures. Published by Centrex Publishing Co., Eindhoven, Netherlands, 1960.

THE HUMAN SPINE IN HEALTH AND DISEASE: ANATOMICOPATHOLOGIC STUDIES. By GEORG SCHMORL, M.D. CLINICORADIOLOGIC ASPECTS. By HERBERT JUNGHANNS, M.D. The first American edition, translated from the fourth German edition, and edited by STEFAN P. WILK, M.D., AND LOWELL S. GOIN, M.D. A volume of 286 pages, with 419 figures. Published by Grune & Stratton, New York, 1959. Price $21.00.

INTUSSUSCEPTION IN INFANTS AND CHILDREN. By MARK M. RAVITCH, M.D., Associate Professor of Surgery, The Johns Hopkins University School of Medicine; Surgeon-in-Chief, The Baltimore City Hospitals, Baltimore, Md. A volume of 122 pages, with numerous figures, including 118 roentgenograms. Published by Charles C Thomas, Springfield, Ill., 1959. Price $9.00.

ENCYCLOPEDIA OF MEDICAL SYNDROMES. By ROBERT H. DURHAM, M.D., F.A.C.P., Physician-in-Charge, Division of General Medicine, Henry Ford Hospital, Detroit. Foreword by T. R. Harrison, M.D., Professor and Chairman, Department of Medicine, Medical College of Alabama, Birmingham. A volume of 628 pages. Published by Paul B. Hoeber, Inc., Medical

Division of Harper & Brothers, New York, 1960. Price $13.50.

LES ISOTOPES RADIOACTIFS. Rapports présentés au XXXII[e] Congrès français de médecine, Lausanne, 1959 (Association des médecins de langue française). Président du Congrès: Professeur A. Vannotti. A volume of 116 pages, with numerous figures and tables. Published by Masson et Cie, 120 Blvd. Saint-Germain, Paris VI[e], France 1959.

Book Reviews

LOW INTENSITY RADIUM THERAPY. BY CHARLES L. MARTIN, E.E., M.D., F.A.C.R., Director of the Martin X-ray and Radium Clinic; Radiologist to Gaston Hospital; Consulting Radiologist to Parkland, Baylor and Veterans Hospitals; Clinical Professor of Radiology, Southwestern Medical School of the University of Texas, Dallas, Texas, and JAMES A. MARTIN, M.D., F.A.C.R., Associate Director of the Martin X-ray and Radium Clinic; Radiologist to Gaston Hospital; Consultant Radiologist to Parkland Hospital; Associate Professor of Radiology, Southwestern Medical School of the University of Texas, Dallas, Texas. A volume of 298 pages, with 20 color plates and 118 black and white illustrations. Published by Little, Brown & Co., Boston, Mass., 1959. Price $12.50.

For many years Dr. Charles Martin has been the most widely known exponent of interstitial radium therapy in the United States. In this monograph, he and his son have collected the technics that have evolved over a number of years and presented them for the guidance of others.

The material is divided into two parts. The first, Technical Considerations, deals with the history of radium therapy and the principles of interstitial therapy, patient care, complications, and radiation hazards. In the second, Clinical Material, various applications of interstitial radium therapy in the treatment of human cancer are presented in the form of illustrated case reports. As would be expected from the nature of interstitial radium therapy, most of the situations described involve tumors of the skin and oral cavity. There are also chapters describing the technic for the treatment of metastatic nodes in the neck, the cervix uteri, the breast, and other situations.

The term low intensity as used in the title is now an anachronism, as the value of radium intensities of 1.0 mg. per centimeter or less in interstitial radium therapy is quite well established. Dr. Martin was a pioneer in the use of this technic in this country, and developed his procedures empirically. This presentation of his methods and results is of interest as it represents the accomplishments of an expert.

RADIOGRAPHIE DU CRÂNE ET DE LA FACE DANS LA MALADIE OSSEUSE DE PAGET. By J.-A. LIÈVRE, Médecin des Hôpitaux de Paris, AND H. FISCHGOLD, Électroradiologiste des Hôpitaux de Paris. A volume of 132 pages, with 75 figures. Published by Masson & Cie, 120 Blvd. Saint-Germain, Paris VI[e], France, 1959. Price 4,000 fr.

In this monograph the authors give a radiological description of the lesions of the skull and facial bones in Paget's disease. The chief interest of the work resides in the thorough study of the involvement of the base of the skull and of the temporal bone.

Seventy-five excellent roentgenograms form the second part of the book, the reproductions being from 25 patients chosen from among 389 affected by this disease. The case histories of this selected group are summarized.

This book can be warmly recommended to radiologists and other specialists interested in the radiographic manifestations of Paget's disease in the skull and facial bones.

DIAGNOSTICA RADIOLOGICA DELLE VIE BILIARI. By T. BRAIBANTI, L. ROSSI, AND A. MAESTRI, Istituto di radiologia dell'Università di Parma. Foreword by Prof. E. Benassi. A volume of 494 pages, with 183 figures. Published by Minerva medica, Turin, Italy, 1958.

This volume is an extraordinarily detailed account of all that pertains to the radiological diagnosis of disease of the gallbladder and bile ducts. In Part I, the authors discuss the preparation of the patient, examination with and without a contrast medium, the use of extrabiliary contrast, special examinations following transparietal and transhepatic contrast injections, postoperative cholangiograms, the study of function, the effects of various drugs on the gallbladder and bile ducts, and the use of roentgen cinematography. The second section of the book includes discussions of congenital anomalies, calculosis, hydrops, cholecystitis, calcification of the walls of the gallbladder, milk of calcium bile, pericholecystic adhesions, tumors of the gallbladder and of the bile ducts. A chapter is devoted to functional disturbances of the biliary tract. Obstruction by extrinsic causes is thoroughly discussed and beautifully illustrated, as are internal and external biliary fistulas. An especially interesting chapter concerns so-called regeneration of the gallbladder following cholecystectomy. This is recognized as actually representing incomplete surgical excision. Ninety pages of bibliography close the book.

In general, this volume is remarkable for the detail with which each subject is discussed. Obviously, the authors have had a great deal of experience in the diagnosis of biliary tract disease, with correlation of their findings with the observations at surgery.

IN MEMORIAM

Charles E. Franklin, M.D.

1904–1960

Dr. Charles E. Franklin of River Forest, Ill., died at his home on Wednesday, Jan. 6, 1960, from a heart ailment. Dr. Franklin was born in Norwood, Ohio, received his M.D. degree from the University of Cincinnati in 1929, and served his internship at the West Suburban Hospital, Oak Park, Ill. Following this he became associated with Dr. R. L. French of Oak Park, and with the Oak Park Hospital, where he assisted in radium and x-ray work for fifteen years. Upon his return from service in the Armed Forces during World War II, he entered private practice as a general practitioner and continued in that capacity until his death.

Dr. Franklin was Past President of the Oak Park Hospital Medical Staff and of the Aux Plaines Branch of the Chicago Medical Society. He was a member of the Illinois State Medical Society, Chicago Roentgen Society, Radiological Society of North America, and the American Medical Association. He belonged to the Oak Park Country Club and the local Rotary Club and was a former deacon in the First Presbyterian Church of River Forest. During World War II, he served as an air force medical officer and spent one year in the Pacific theater of operations.

Surviving Dr. Franklin, are his wife, the former Elva Erlenborn, to whom he was married twenty-seven years ago, and two daughters, Mrs. Sally Besinger of Carpentersville, Ill., and Mrs. Susan Laage of Oak Park, Ill.

Dr. Franklin was loved and respected by all with whom he came in contact. He was an excellent radiologist and practiced the very highest type of internal medicine. ROBERT L. FRENCH, M.D.

ABSTRACTS OF CURRENT LITERATURE

ROENTGEN DIAGNOSIS

The Head and Neck

The Chest

The Heart and Blood Vessels

The Digestive System

The Musculoskeletal System

Gynecology and Obstetrics

The Genitourinary System

The Lymphatics

Miscellaneous

RADIOTHERAPY

RADIOISOTOPES

RADIATION EFFECTS

ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Metopism and Its Correlation with the Development of the Frontal Sinuses. A Roentgen-Anatomic Study. Roman Marciniak and Czeslaw Nizankowski. Acta radiol. **51:** 343–352, May 1959. (Medical Academy, Wroclaw, Poland)

The relationship between persistence of the metopic suture and development of the frontal sinuses was investigated in the skull films of 2,018 living patients. A persistent metopic suture was found in 252 cases (12.5 per cent). In 20 of these, or 8 per cent, there was bilateral absence of the frontal sinuses and in 18, or 7 per cent, unilateral absence of a frontal sinus.

Museum material consisting of neolithic and diluvial skulls was also studied. Of 352 neolithic skulls, 26 (7.4 per cent) showed a persistent metopic suture, and bilateral frontal sinuses were present in 21 of the 26. A persistent metopic suture was found in 67 (5.9 per cent) of 1,042 diluvial skulls.

The authors conclude that persistence of the metopic suture is not related to underdevelopment or absence of the frontal sinuses. Apparently, the persistent metopic suture is an expression of evolution, because of the higher incidence of this feature in neolithic skulls than in diluvial skulls.

Two roentgenograms; 3 tables.

SAMUEL B. HAVESON, M.D.
Lynwood, Calif.

A Lateral Medullary Syndrome Following Vertebral Angiography. Bryan Ashworth and W. M. C. Allen. Brit. J. Radiol. **32:** 342–343, May 1959. (Crumpsall Hospital, Manchester, England)

The authors present the case of a 26-year-old male with a lateral medullary syndrome following left vertebral angiography and still persisting at the time of the report, six months later. Two injections of 16 c.c. of 60 per cent Urografin each were given in the vertebral artery during the procedure. Approximately two weeks earlier, the patient had undergone bilateral carotid angiography without ill effect. The symptoms which developed after the vertebral angiography were apparently due to occlusion of the posterior inferior cerebellar artery on the left side.

Several cases of transient complications of vertebral angiography are cited from the literature.

J. S. ARAJ, M.D.
Toledo, Ohio

Carotid Angiography with Tri-Iodobenzoic Acid Derivatives. A Comparative Experimental Study of the Effects on the Systemic Circulation in Cats. Percy Lindgren. Acta radiol. **51:** 353–362, May 1959. (Karolinska Institutet, Stockholm, Sweden)

Changes in arterial blood pressure and heart rate following carotid arterial injection of Triurol (sodium acetrizoate), Hypaque (sodium diatrizoate), and Miokon (sodium diprotrizoate) were investigated in a series of 12 cats. The amount of contrast material injected was comparable to quantities used in human carotid arteriography. Triurol [which is similar to Urokon] caused an average decrease in heart rate of 24 per cent and an average drop in blood pressure of 25.5 mm. Hg. The decrease in heart rate and blood pressure was considerably less marked following injection of Hypaque or Miokon. Hypaque caused an average decrease of 6.5 per cent in pulse rate and an average fall of 10.3 mm. Hg in blood pressure. The average figures for Miokon were almost identical with those for Hypaque. In each instance, there was a latent period of two or three seconds, before the effects on heart rate and blood pressure occurred.

Clinically, even a moderate fall in blood pressure and mild bradycardia may be deleterious since the time during which the vascular endothelium is exposed to the contrast material may be prolonged. Toxic effects might further be enhanced by a short latent period because more contrast material would be present in the vessels during the phase of bradycardia and lowered blood pressure. Triurol has been shown to cause far more damage to the blood-brain barrier than Hypaque (Whiteleather and DeSaussure: Radiology **67:** 537, 1956; Lindner, D. W. *et al.* Surg. Forum 7: 553, 1957).

Five figures.

SAMUEL B. HAVESON, M.D.
Lynwood, Calif.

Radiography in Diagnosis of Maxillo-Facial Injuries. Mulk Raj. Indian J. Radiol. **13:** 71–76, May 1959. (Armed Forces Medical College, Poona, India)

The subject of injuries to the maxillofacial region is discussed from the point of view of the surgeon. A detailed description of the various roentgen studies of this region with the views and technics is given. Positioning for best demonstrations of the injuries at different sites is outlined. The views, technics, and fractures are already familiar to radiologists.

One diagram.

J. S. ARAJ, M.D.
Toledo, Ohio

Cineradiographic Studies of Glossopharyngeal Breathing. G. M. Ardran, W. Howlett Kelleher, and F. H. Kemp. Brit. J. Radiol. **32:** 322–328, May 1959. (Western Hospital, Fulham, London, England)

The authors investigated glossopharyngeal breathing by cineradiography in patients who had respiratory difficulties associated with limitation or paralysis of one or both leaflets of the diaphragm. This type of respiration appears to have first been observed by Dail (see, for example, California Med. **75:** 217, 1951; J.A.M.A. **158:** 445, 1955).

The present writers found that although glossopharyngeal breathing resembles swallowing in some respects it is not identical. One of the principal features of swallowing, the pharyngeal constrictor peristaltic wave, is absent. The authors believe that cineradiography is a useful method for determining why some patients do not acquire this technic of breathing.

Fifteen roentgenograms; 1 chart; 1 table.

THEODORE E. KEATS, M.D.
University of Missouri

THE CHEST

Chronic Bronchitis and Emphysema: A Symposium. I. The Epidemiology of Chronic Bronchitis. C. H. Stuart-Harris. Brit. J. Radiol. **32:** 286–289, May 1959. (University of Sheffield, Sheffield, England)

Chronic bronchitis, however defined, is neither a static nor yet a slowly progressive disturbance. It

develops with increasing frequency as age advances and affects men to a greater extent than women. Its course is one of intermittent illnesses suffered chiefly in the winter, from which recovery is progressively more difficult and which ultimately leads to death. The effects of these illnesses are probably more marked in those who are heavy smokers or who live in an industrial environment or who work in certain occupations with exposure to dust than in nonsmokers, rural dwellers, or those whose work is of a cleaner character. But epidemiological data alone do not enable one to say whether the state of being subject to harm as a result of acute lower respiratory infections or of smogs is some residue from a former illness, or is attributable to a diathesis inbred and genetically determined from the moment of conception.

Abstracts of Parts II and III of this symposium follow.

Four tables.

THEODORE E. KEATS, M.D.
University of Missouri

Chronic Bronchitis and Emphysema: A Symposium. II. Clinical Aspects of Chronic Bronchitis. Neville C. Oswald. Brit. J. Radiol. **32:** 289–290, May 1959. (St. Bartholomew's Hospital, London, England)

The clinical course of chronic bronchitis may extend over many years. The onset is usually insidious, with a tendency for colds to go down to the chest in the winter months. In a minority of people in whom this occurs, cough and sputum following a cold become a regular feature in cold, damp weather. A further minority proceed to chronic bronchitis with a persistent cough and sputum in the winter and later all the year round. At any stage in this process bronchospasm may be superimposed. If infection is added to the extent that a purulent sputum occurs, the lungs are likely to be damaged by progressive emphysema. Eventually, death may occur from bronchopneumonia, right heart failure, or anoxia.

From a therapeutic standpoint, regard must be paid to the relative importance of excessive mucus, bronchospasm, infection, and emphysema. Treatment for excessive mucus is largely prophylactic, that is, the avoidance of factors which stimulate further production. Antispasmodic drugs, including steroids, help in relieving bronchospasm. For the infection, a rapid and favourable response can usually be obtained in acute exacerbations by a combination of penicillin and streptomycin. In less acute attacks and during remissions the tetracycline drugs are often valuable. Emphysematous patients may be aided by exercises, in which lateral thoracic expansion and diaphragmatic breathing are encouraged.

For Part I of this symposium, see preceding abstract. Part III is abstracted below.

THEODORE E. KEATS, M.D.
University of Missouri

Chronic Bronchitis and Emphysema: A Symposium. III. Pathological Findings and Radiological Changes in Chronic Bronchitis and Emphysema. Lynne Reid and G. Simon. Brit. J. Radiol. **32:** 291–305, May 1959. (Brompton Hospital, London, S. W. 3, England)

Pathological Findings in Chronic Bronchitis (Reid): In the well established case of chronic bronchitis the hypersecretion is reflected by a hypertrophy of the mucous glands and the goblet cells. The ducts of the glands become dilated and pit-like and may be outlined in the large bronchi in bronchograms. The present hypothesis is that this hypersecretion with hypertrophy of mucous glands may be caused by a number of different irritants, which may act together.

Infection is probably the most important single factor in causing permanent destruction and distortion of the bronchi and bronchioles. The large bronchi may then show changes of acute bronchitis, infiltration with inflammatory cells, and varying degrees of damage to the epithelium, even to complete destruction. The infection may involve the alveoli as well, with a picture of bronchopneumonia. Acute infection may subside and leave permanent damage of two types. The first is destruction of tissue, which affects walls of bronchioles but more particularly the alveolar tissue, giving rise to one type of emphysema. The second is fibrosis or scarring, which may cause localized stenosis and irregularity of bronchiolar lumina or may implicate a considerable volume of lung, condensing bronchioles and alveoli into a dense scar.

Evidence of peripheral damage to the bronchial tree is more easily detected in a bronchogram than in a plain roentgenogram. Bronchioles ending blindly in scars usually have irregular, tapering, or rounded endings, and the peripheral pattern of such pathways is lacking. Small bronchi or bronchioles may be dilated, forming "pools" of radiopaque material, often rounded or lobulated. This bronchiolectasis may represent dilatation from ulceration of bronchiolar walls, or the structure of the wall may be intact, but the airway dilated within a scar. The bronchiole is usually obliterated beyond the point of obstruction. It may have one or more spikes to its outline representing side branches which have shared in the dilatation and obliteration.

Radiological Changes in Chronic Bronchitis (Simon): A chest radiograph of a person suspected of chronic bronchitis may show only slight or perhaps no abnormalities. In some cases there are isolated tubular shadows, with or without a central translucency, or small ring shadows, occupying only a small part of the lung fields, indicating an accompanying bronchiectasis. Such a bronchiectatic area may aggravate or even initiate a generalized bronchial disease, but is more probably an incidental complication, being quite common in an elderly bronchitic.

Small ill-defined homogeneous shadows, roughly circular in shape, were also seen in many patients, usually only one or two at a time and those often in the upper third of the lung. These are often dismissed as old tuberculous foci, but it seems probable that many of them represent nontuberculous fibrotic scars or nodules. A less frequent finding was widespread honeycomb or reticular shadowing in the lower halves. Other changes seen with some frequency were old pleural thickening, old apparently tuberculous scars, localized lobar or segmental bronchiectasis, and emphysema.

A bronchogram, unlike a plain roentgenogram, usually shows a considerable number of abnormalities in a chronic bronchitic. A common finding is that of small spiky projections from the undersurface of the main or segmental bronchi. These projections represent contrast medium in the pit-like depressions formed by the abnormal openings of the mucous gland ducts. A much less common finding is an excessive change in the caliber of a bronchus. This may be mainly the result of abnormalities in the surrounding lung tissue rather than of destructive changes in the wall of the

bronchus itself. Similarly a concertina-like deformity with slight widening of the lumen is probably due in part to shortening of the bronchus from condensation of the surrounding pulmonary tissue.

Much more frequent and characteristic of chronic bronchitis are occlusions of the bronchi after about five to eight generations along an axial pathway, or of the bronchioles still more distally. The ending of the contrast medium may be clear-cut and even, with parallel walls, like a broken bough. This appearance will suggest a functional obstruction to the more distal flow of the medium, whether from excessive secretion in the lumen or from air trapping and absence of the normal inspiratory suck, resulting from occlusion of that pathway at a more distal level. An organic occlusion will be probable if the ending is more tapering in form. Sometimes there is a slight dilatation preceding first a narrow area and then the occlusion. Sometimes the bronchus ends in a bulbous expansion. In all these forms of occlusion there is absence of peripheral filling.

Another common finding is the abrupt ending of the contrast medium in a small circular pool at the end of a narrow branch 2 to 3 mm. long. Such a pool represents a dilated bronchiole and may vary in diameter from 2 mm. to a centimeter or more.

The presence of these bronchial abnormalities will indicate considerable damage to the peripheral bronchioles and is very suggestive but not conclusive evidence of chronic bronchitis. Occasionally the more distal pathways show some distortion of their course around bullae, and in such cases the distorted bronchus shows fewer branches than normal.

Pathological Findings in Emphysema (Reid): The author classifies emphysema in two groups. In *Group I*, or dilatation emphysema, the respiratory unit is distended but anatomically intact. This group includes spasmodic asthma and compensatory emphysema, obstructive emphysema, simple coal-miner's pneumoconiosis, senile emphysema, and the dilatation emphysema associated with chronic bronchitis. In *Group II*, destruction emphysema, there is some degree of destruction, which may even be complete so that no residue of a respiratory unit can be recognized (a bulla). It is in this group that serious disability may occur. Infection plays an important role in the production of destruction emphysema. Once destruction of tissue has occurred, retraction of the surrounding elastic lung increases the size of the lesion and gives it a characteristic, roughly spherical shape. Other sequelae of destruction are loss of the capillary bed, interruption of the blood supply to the distal part of the acinus, and transformation of the wall of the bronchiole into the structure of a flap-valve. The loss of integrity in a large part of the lung is one of the main causes of trapping of air in the lungs, which gives rise to an increase in lung volume, diminished movement of a low flat diaphragm, and increased translucency.

Certain situations predispose to enlargement of an individual lesion. In the subpleural region the flap-valve cannot equalize between neighboring units because of the presence of connective tissue septa which are not evenly distributed throughout, but are localized particularly in the subpleural region. Such air collections are usually described as bullae. Large collections of air often cause compression of surrounding lung, either of that immediately adjacent to the bulla or of the remainder of the lobe or lung.

In small destructive lesions within an acinus the blood vessels are too small to be seen directly in a radiograph, but loss of the capillary bed will contribute to an increase in translucency. Radiographically, the most characteristic feature in emphysema is the enlargement of the main pulmonary arteries with abrupt reduction in the size of their branches right from their source. The main pulmonary artery seems to act as a reservoir of blood, while the intrapulmonary branches reflect the increased intrapulmonary pressure in emphysema. The pulmonary artery branches supplying scars and in the region of bullae may show endarteritis obliterans.

Radiological Changes in Emphysema (Simon): A roentgenogram may show the following changes in emphysema:

1. *Hypertranslucency:* Hypertranslucency may be diffuse or localized, as is often the case in chronic bronchitis.

2. *Diaphragm Changes:* The lungs occupy more space than normal and this is shown in the roentgenogram by the low position of the diaphragm and the wide anteroposterior diameter of the chest, together with a widened retrosternal translucency in the lateral view. The diaphragm shows poor movement on respiration.

3. *Bullae and Bullous Areas:* Gross local distention of the lung, particularly in the subpleural region, associated with alveolar disruption is characteristic of a bulla. This is often visible radiographically as a hypertranslucent avascular zone with a hair-line shadow marking its limits. This hair-line represents the margin of compressed lung, pleura, or septa. Where the air distention is very gross in some localized area, the local vessels are lost because of the disruption of pulmonary tissue, and the vessels in the nearby lung are pushed aside. These abnormalities will be visible on the roentgenogram, the vessels being sometimes so crowded together around the air space as to give an almost reticular pattern.

4. *Cardiovascular Changes:* The reduction in the amount of capillary blood mentioned above may be due solely to the air occupying more space, and the blood being therefore more spread out, but in most cases there is an additional loss of capillary bed due to destruction of the lung tissue. Pulmonary hypertension is common and may be responsible in part for the pulmonary vessel changes. Often the main trunk of the pulmonary artery is dilated. In contrast to the larger vessels, the major intrapulmonary vessels tend to appear small and inconspicuous in spite of the high contrast afforded by the excessive amount of air in the alveoli around them. The peripheral vessels are inconspicuous and may be fewer in number.

Two facts stand out in connection with chronic bronchitis and emphysema: first, when the initial radiograph is available, there is frequently a long history of cough and sputum, often covering twenty years or more; second, the roentgenogram may change even over a period of five years, during which time the patient often experiences increasing breathlessness on exertion.

In cases where all the radiographic changes are present, the x-ray diagnosis of emphysema is reasonably accurate. When only some of the changes are present, or these are slight, the diagnosis may be less certain. Correlation with the clinical findings is not always very close, but tends to be closer when the x-ray appearances

are assessed in relation to their probable physiological consequences.

For Parts I and II of this symposium, see above.

Thirteen roentgenograms; 6 photomicrographs; 4 photographs; 4 diagrams.

THEODORE E. KEATS, M.D.
University of Missouri

Great Vessel Involvement in Lung Cancer: Angiocardiographic Report on 250 Consecutive Proved Cases. Israel Steinberg and Nathaniel Finby. Am. J. Roentgenol. **81:** 807–818, May 1959. (New York Hospital-Cornell Medical Center, New York, N. Y.)

Angiocardiography is useful in evaluating lung cancer, for results of this study provide indications of resectability and prognosis and may influence the surgical management of a given case. For visualization of the superior vena cava and pulmonary arterial circulation it is necessary to obtain frontal angiocardiograms. If the superior vena cava is affected, right lateral projections are made. Anterior oblique views demonstrate the major pulmonary arteries and their branches.

One hundred cases of lung cancer in which angiocardiography was employed were previously reported (Steinberg and Dotter: Arch. Surg. **64:** 10, 1952. Abst. in Radiology **59:** 764, 1952). This series is now increased by 150 additional cases.

The angiocardiographic findings are classified in five groups: (1) no pulmonary vascular changes (27 of the 150 cases constituting the new series and 40, or 16 per cent of the combined series); (2) involvement of the superior vena cava system (14 new cases, 31 of combined series, or 12 per cent); (3) major pulmonary artery involvement (21 new cases, 46 of combined series, or 18 per cent); (4) lobar and segmental pulmonary artery involvement (87 new cases, 131 of combined series, or 53.2 per cent); (5) pericardial invasion (1 new case, 2 of combined series, or 0.8 per cent). Involvement of the superior vena caval system varied from polypoid invasion to partial or complete occlusion by adjacent masses.

In 30 per cent of the 250 cases, superior vena caval and major pulmonary arterial involvement were disclosed. This occurred most often in association with hilar and mediastinal tumors. Involvement of these vessels is an indication that the tumor is not resectable. In the absence of serious great vessel involvement, the pulmonary lesion is usually regarded as operable. If the vascular deformity is confined to a segment or lobe, lobectomy rather than pneumonectomy may be feasible.

Angiocardiography is not to be employed as the primary diagnostic tool in establishing the presence of lung cancer; its utility lies in preoperative determination of operability.

Thirty-four roentgenograms; 1 table.

JOHN W. WILSON, M.D.
Johnstown, Penna.

Segmental Atelectasis in Children with Primary Tuberculosis. Simon Frostad. Am. Rev. Tuberc. 79: 597–605, May 1959. (Grefsen Sanatorium, Oslo, Norway)

This report discusses the findings in 90 children with primary tuberculosis in whom segmental atelectasis was noted. Bronchoscopy was done on all of the patients. Bronchial stenosis caused by lymph node perforation was found in 78.8 per cent of the series. Changes such as the presence of granulation tissue, scar tissue, and purulent secretion from one or more bronchial ostia were found in others. In only one patient was bronchoscopic examination negative. All but 4 of the children received chemotherapy, the majority being on triple drug therapy (streptomycin, isoniazid and PAS).

In 33 cases bronchograms were obtained at the end of the therapy period. Abnormalities were found in 27. These consisted of bronchiectasis, bronchial stenosis, dislocation of bronchial branches and changes in bronchial walls. Bronchostenosis was the most common, occurring in 16 patients, with bronchiectasis noted in 12. These bronchograms indicate the high incidence of residual bronchial changes in patients in whom atelectasis complicated primary tuberculosis. The segmental atelectasis was more common in the right lung than in the left, and most of the lymph node perforations were on the right, usually in the vicinity of the middle lobe orifice or slightly, above.

In addition to chemotherapy, resection of 31 segments was done in 15 children with segmental atelectasis. Pathologic findings were those of progressive tuberculosis in the segments of 12 of the patients, with persistent cavitation in 3. Other findings were fibrosis, atelectasis, and bronchiectasis.

Two figures; 8 tables.

JOHN H. JUHL, M.D.
University of Wisconsin

Problems Raised by Unilateral Pulmonary Radiolucencies with Hypovascularization. G. Brouet, J. Chevallier, M. Vasselin, and M. Castillon du Perron. J. franç. de méd. et chir. thorac. **13:** 481–509, 1959. (In French) (Paris, France)

The authors report 5 cases in which one lung was found to be radiolucent on a routine chest survey or examination for minor respiratory conditions. The patients were men from twenty-five to fifty years old.

Hypovascularity of the radiolucent lung was shown by angiography. Spirometry revealed a reduction in ventilation with a great decrease in the consumption of oxygen. Bronchiectasis was associated with the vascular disturbances in 4 cases.

Various etiopathogenic mechanisms have been suggested to explain this particular syndrome, as congenital anomaly of the pulmonary artery or acquired disturbances of the pulmonary circulation, which could be derived from thrombosis or arterial compression or be secondary to hypoventilation and bronchiectasis. Two hypotheses have commanded the attention of the authors: congenital arterial hypoplasia; vascular and bronchial disturbances associated in the framework of hilar disease, going back to a primary tuberculous infection.

Eighteen roentgenograms.

RENÉ HOURI, M.D.
New York, N. Y.

THE HEART AND BLOOD VESSELS

The Roentgenologic Features of Ebstein's Anomaly of the Tricuspid Valve. Kurt Amplatz, Richard G. Lester, Gerold L. Schiebler, Paul Adams, Jr., and Ray C. Anderson. Am. J. Roentgenol. **81:** 788–794, May 1959. (University of Minnesota, The Medical School, Minneapolis 14, Minn.)

Plain-film roentgenography can often provide a

correct diagnosis of Ebstein's anomaly. In this malformation, there is downward displacement of the tricuspid valve from the true annulus. Varying widely, the valve leaflets may be large, rudimentary, or almost totally absent. They may be thick and nodular or thin and perforated. The leaflet material may be adherent to the endocardium. The papillary muscles and chordae tendineae are malformed. The ventricular musculature is thin, and there is dilatation of the right ventricular outflow tract.

The clinical features vary, probably in accord with the variable degrees of deformity of the tricuspid valve. This deformity may result in stenosis or insufficiency, or the hemodynamics may be fairly normal. Dyspnea, fatigue, squatting, tachycardia, and cyanosis are common. Characteristically, cyanosis is mild in the neonatal period, following which it disappears, with subsequent recurrence later in childhood or in adult life. Cyanosis and decreased pulmonary circulation result from a right-to-left shunt through an incompetent foramen ovale. The malformation may be associated with systolic and diastolic murmurs, "triple" or "quadruple" rhythms, and a right bundle branch block or Wolff-Parkinson-White pattern on the electrocardiogram. The average life expectancy is between twenty and thirty years of age.

Radiographically the cardinal features are marked cardiac enlargement as a result of massive dilatation of the right heart. The pulmonary vascular volume is normal or decreased, and, in spite of gross cardiomegaly, pulmonary congestion is strikingly absent. With dilatation of the outflow tract of the right ventricle, there is a bulging of the left heart border horizontally toward the left chest wall. The right atrium may dilate to form the posterior heart contour in the left anterior oblique and lateral projections. These configurations are responsible for the box-like silhouette of the heart in Ebstein's malformation. Milder cases may show only a "sloping" of the left heart border resulting from the posterior displacement of the left ventricle by the dilated right heart. In some cases the cardiac contours are normal.

Cardiac catheterization is the most satisfactory method of identifying Ebstein's anomaly, particularly in the earlier stages, before the characteristic late manifestations are recorded radiographically.

Eleven roentgenograms; 1 diagram.

JOHN W. WILSON, M.D.
Johnstown, Penna.

Costal Intra-Osseous Angiocardiography. Robert Schobinger, Joseph Stein, and Philip Cooper. Acta radiol. **51:** 337–342, May 1959. (VA Hospital, Bronx 68, N. Y.)

Satisfactory demonstration of the cardiac chambers and great vessels was obtained by injection of contrast material into the medullary cavity of the 4th, 5th, 6th, or 7th rib in the right anterior axillary line. Fifty cubic centimeters of 50 per cent Hypaque was manually injected through plastic tubing attached to a 16-gauge Rosenthal bone-marrow needle placed in the medullary cavity of the rib. Correct positioning of the needle is confirmed by aspiration of bone marrow accompanied by a subjective feeling of "pressure." The average injection time was eight seconds.

Filling of the heart occurs primarily *via* the internal mammary and subclavian veins if the 4th rib is injected. Injection of the 5th rib outlines the lateral thoracic vein joining the axillary vein, the intercostal veins leading anteriorly to the internal mammary vein and posteriorly into the upper portion of the azygos vein through the paravertebral veins. The heart fills primarily *via* the ascending azygos vein when the 7th rib is injected.

The technic described is useful when selective angiocardiography or the usual intravenous method is not feasible.

Five roentgenograms; 2 photographs.

SAMUEL B. HAVESON, M.D.
Lynwood, Calif.

Cinecardiometry and Cine-Electrokymography. New Angiographic Techniques for the Analysis of Cardiac Mechanics. Frank L. Campeti, with the technical assistance of Vivian A. Palladoro. Am. J. Roentgenol. **81:** 778–787, May 1959. (University of Rochester School of Medicine and Dentistry, Rochester, N. Y.)

Cinecardiometry is a method of recording motion of cardiovascular structures opacified by a contrast medium. The borders of heart chambers and great vessels are drawn directly from projected images of each frame of a cineangiocardiogram and the diameters and areas are measured chronologically from these drawings. From these, volumes of the cardiac cavities can be calculated. Each measurement of each class of diameters, area, and volume, expressed as a percentage of the arithmetical average of the whole class, is recorded on graph paper, being plotted on the ordinate against time. By joining these points, continuous curves are drawn.

Densitometry is a photometric method for recording angiographic density of the cardiovascular structures from each frame of a cineangiocardiogram. By plotting each volume chronologically on the ordinate against time, a continuous curve can be traced. Curves recorded from the same film, in different parts of the cardiovascular system, can represent the progression and distribution of contrast medium peripherally injected into the great vessels and cardiac cavities.

Cine-electrokymography and *cine-densitometry* are electrokymographic technics for recording the border motion and density changes of the cardiovascular structures from a cinefluorogram projected on the screen.

Correlation of these tracings recorded by the above technics with electrocardiograms, pressure studies, pneumograms, etc., recorded synchronously with the cineangiocardiogram can represent cardiac performances in each phase of the cardiac cycle.

Since these cineroentgenologic methods provide details of cardiac mechanics and hemodynamics, they are useful in physiologic investigations and in selected cases of cardiac physiopathology.

Seven graphs.

JOHN W. WILSON, M.D.
Johnstown, Penna.

The Development and Anomalies of the Aortic Arch and Its Branches, with the Report of a Case of Right Cervical Aortic Arch and Intrathoracic Vascular Ring. H. R. S. Harley. Brit. J. Surg. **46:** 561–573, May 1959. (Cardiff Royal Infirmary, Cardiff, Wales)

This is a very detailed article which reports a case of an anomalous right aortic arch presenting in the right side of the neck to the level of the mandible. The patient was first seen in 1937 at the age of five years, with a mass in the right neck thought to be aneurysm

of the right common carotid artery. The true nature of his condition was discovered during exploration in 1939. Dysphagia developed in 1957 and esophageal study revealed indentation of the posterior wall of the esophagus in its middle third. This was found to be due to a vascular ring formed by the retro-esophageal segment of the aorta behind, the ligamentum arteriosum on the left side, and the division of the pulmonary artery and its left branch in front.

The remainder of this article deals at length with the embryological development of the aortic arches, the aorta, and its branches. The various vascular anomalies or combinations of anomalies which may compress the trachea, esophagus, or both are listed and illustrated. Differential features distinguishing aneurysm of the right common carotid and aorta presenting in the neck, as in the reported case, are enumerated. These include the age of the patient (aneurysms are unusual in childhood); the type of pulsation; the effect of compression of the pulsating swelling on the peripheral arterial pulses; presence or absence of evidence of a vascular ring in the thorax. Finally, the two conditions may be differentiated by angiography. This procedure clearly demonstrated the arch of the aorta in the neck in the author's case. Radiological diagnosis and surgical treatment of various vascular anomalies of the aorta and its branches are discussed.

Five roentgenograms; 26 diagrams.

J. S. ARAJ, M.D.
Toledo, Ohio

Aortography and Peripheral Arteriography: An Analysis of Results in a University Medical Center. John H. Foster and Duncan A. Killen. Ann. Surg. **149**: 321–341, March 1959. (Vanderbilt University School of Medicine, Nashville, Tenn.)

All aortograms and peripheral arteriograms (excluding cerebral arteriograms) obtained from 1950 through 1957 at Vanderbilt University Medical Center (Nashville, Tenn.) were reviewed. Of 25 thoracic aortographic studies in 24 patients, 18 (72 per cent) were diagnostic. In 2 of this series minor complications developed. Of 127 abdominal aortographic examinations in 117 patients, 89 (70 per cent) were diagnostic. In this group 14 complications occurred. Eighty-one peripheral arteriograms were obtained in 63 patients and 52 (64 per cent) were diagnostic: there were 3 cases with complications. There was thus a total of 233 procedures in 204 patients, with diagnosis in 159 (68 per cent). Four major complications occurred: 2 after percutaneous femoral arteriography and 2 following translumbar abdominal aortography. Reports of these cases are included. A case of paraplegia and one of femoral artery thrombosis seem to have been direct results of the procedure; a popliteal artery thrombosis may have represented coincidental progression of the disease process; death of a patient with severe renal disease may have been due to other causes.

Thoracic aortography is considered useful in the demonstration of aneurysm, dissecting aneurysm, and occasional atypical cases of coarctation of the aorta or patent ductus arteriosus. Abdominal aortography is indicated in renal hypertension, arteriosclerotic narrowing of the terminal aorta, and suspected abdominal aortic aneurysm; it is of little value in abdominal aneurysm or complete arteriosclerotic occlusion of the terminal aorta. Peripheral arteriography is worthwhile in aneurysm, arteriovenous fistula, and occlusive disease; segmental occlusive disease and the adequacy of the distal run-off are most accurately determined by this method, sometimes solely by its use.

The following suggestions, grouped for convenience under five headings, are made for obtaining successful yet safe arteriograms. Those thought to be of greatest importance are marked with an asterisk.

With *injection technic*, there should be a single injection of medium;* meticulous needle insertion technic;* prone position for abdominal aortography; a needle of minimum caliber (#18 for abdominal aortography); good equipment, checked prior to use; measures to impede rapid run-off; rapid manual injection (automatic injection with catheters); injection above or below the renal arteries in abdominal aortography; removal of needle immediately following injection; meticulous closure of arteriotomies; carotid compression in thoracic aortography; hydration of patient prior to aortography.

The *anesthesia* should be local whenever possible;* if general anesthesia is necessary, endotracheal intubation should be employed; there should be minimum movement of the patient once the needle is inserted.

The *contrast medium* of least toxicity (currently Hypaque 50 to 90 per cent solution) should be employed,* and in minimum quantity; it should be warmed to body temperature and there should be sensitivity testing.

The *x-ray technic* should provide for rapid serial exposures or prolonged exposure* and scout films.

In respect to *patient predisposition*, there should be greater selectivity of patients for arteriography;* careful consideration of a history of allergy; avoidance of direct puncture of aneurysms; recognition of added risk in patients with azotemia, bleeding tendency, hypertension, or with cardiac, pulmonary, or cerebral disease.

Seventeen roentgenograms; 4 charts and diagrams; 13 tables.

Inferior Mesenteric Artery Occlusion Following Lumbar Aortography. R. F. C. McDowell and I. D. Thompson. Brit. J. Radiol. **32**: 344–346, May 1959. (The Queen's University of Belfast, Belfast, Ireland)

An unusual complication of abdominal aortography in a 40-year-old man with Leriche's syndrome is here reported. The medium, 70 per cent Diodone, was introduced at the level of the third lumbar vertebra. An initial injection of 5 c.c. to localize the tip of the needle was followed by two injections of 30 c.c. each. Evidence of a thrombus at the aortic bifurcation was obtained; there was considerable retrograde filling of the aorta, and the medium was seen to enter the mesenteric artery, probably due to the block at the aortic bifurcation.

After recovery from the anesthesia, the patient complained of abdominal pain; distention developed in twenty-four hours, and bloody stools were passed on the fourth day. Finally, complete obstruction ensued and a transverse colostomy was performed forty days after aortography. A week later 2 feet of necrotic colon was passed per rectum.

The authors suggest the following precautions in the performance of lumbar aortography: (1) A repeat injection should be avoided when discharge from the aorta is delayed. (2) If a Leriche syndrome is suspected

clinically, not more than 20 c.c. of contrast medium should be used, and a lower concentration (45 per cent Hypaque or 60 per cent Urografin) should be selected. (3) A high aortic puncture should be made. It is pointed out that, though a small test injection may prove the needle tip to be in the lumen of the aorta, it is unlikely to give warning of shunting of the medium into visceral arteries.

One roentgenogram; 1 photograph; 1 drawing.

J. S. ARAJ, M.D.
Toledo, Ohio

Collateral Circulation Between a Spleen Transposited into the Thoracic Cavity and the Vena Cava Superior: Significance in Portal Decompression. Martti Turunen and Heino Laitinen. Ann. Surg. **149:** 443–447, March 1959. (Kivelä Hospital, Helsinki, Finland)

Three cases of portal hypertension complicated by esophageal varices were treated by transposition of the spleen into the thoracic cavity in the hope of producing portal decompression as a result of collateral circulation between the spleen and the superior vena cava. For management of the acute hemorrhage from which the patients were suffering, part of the esophageal varices were ligated and thrombosed in 2 patients. Bleeding was arrested in all cases and did not recur. Splenoportography eight months to four years later revealed collateral circulation between the transposed spleen and superior vena cava, directly proportional to the preoperative severity of the varices. In Case II, in which the varices were mildest, the roentgenograms disclosed collaterals of almost capillary size between spleen and pleura; In Case III there was between the two organs a large venous plexus from which the contrast agent was seen to pass upward along the enlarged intercostal vein; in Case I, numerous venous plexuses had developed between spleen and pleura and from these the medium passed along several intercostal veins to the hemiazygos and the left subclavian vein. In all 3 cases the roentgenograms showed enlargement of the portal veins, evidently due to continued hypertension. Thus it appeared that collaterals developed only in numbers sufficient to arrest the gastroesophageal hemorrhage.

After transposition the spleen shrank in size and no symptoms of splenomegaly occurred. The operation is a relatively safe procedure and may be performed on patients in poor condition.

Transposition of the spleen does not, to the same extent as the portocaval shunt, stop the circulation through the liver in patients with portal hypertension. This is considered an advantage.

Six roentgenograms.

Normal Pulsations in the Pulmonary Vascular Tree as Seen with Roentgenoscopic Image Amplification. Brit B. Gay, Jr. Am. J. Roentgenol. **81:** 801–806, May 1959. (Emory University School of Medicine, Atlanta, Ga.)

With conventional fluoroscopy pulsations in the smaller branches of the pulmonary arteries are not demonstrable. When, however, the fluoroscopic image is increased in brightness by image amplification, the pulsations become visible. The author reports a study of variations in pulmonary artery pulsations determined by this means in 100 normal subjects. It is pointed out that the data thus obtained are based entirely upon subjective impressions.

Studies of the pulsations in the pulmonary arteries were recorded at five locations: (1) the main pulmonary artery segment of the left heart border; (2) the left pulmonary artery branch as it descends through the left hilus; (3) the right descending pulmonary artery branch in the right hilus; (4) the peripheral segmental branches of the left pulmonary artery in the basilar divisions of the left lower lobe; (5) the peripheral segmental branches of the right pulmonary artery in the basilar divisions of the right lower lobe.

Pulsations of the right descending pulmonary artery branch were always easily visible in normal patients at rest. The amplitude was slightly variable. Exercise increased the prominence of the pulsations only slightly. In following this arterial branch inferiorly into the segmental arterial trunks to the middle and lower lobes, pulsations become more difficult to visualize. Pulsations in the basilar arteries of the right lower lobe are not usually visible, so that well defined expansile activity in these trunks is considered abnormal.

Pulsations in the left pulmonary artery branch in the hilar region are usually more prominent than those seen in the right descending pulmonary artery branch. Sometimes the difference in the amplitude of pulsation of these two arteries is striking. In isolated valvular pulmonary stenosis the pulsations of the right ascending pulmonary artery became hypoactive and the pulsations in the left descending branch became hyperactive. Basilar vascular divisions of the left pulmonary artery are also more readily visualized normally than similar branches on the right. Pulsations of the branches of the upper lobe segments of both lungs and pulsations of the main pulmonary artery at the left heart border are poorly defined and variable, respectively, and are considered of no value in determining changes in pulmonary circulation.

The pulsatile activity of the smaller basilar branches of the pulmonary arteries is increased with exercise, with expiration, and with the Müller maneuver and decreased in inspiration and with the Valsalva maneuver. Pulsations of the segmental pulmonary arterial branches are obscured in the presence of heart failure.

Three roentgenograms; 2 diagrams.

JOHN W. WILSON, M.D.
Johnstown, Penna.

Roentgenographic Signs of Pulmonary Artery Occlusion. Daniel J. Torrance, Jr. Am. J. M. Sc. **237:** 651–662, May 1959. (Johns Hopkins University School of Medicine, Baltimore, Md.)

The radiographic signs of pulmonary artery occlusion are discussed under seven headings, and the distinction between occlusion with and without infarction is emphasized.

(1) Most frequently there is *no demonstrable abnormality* on the film. In order for pulmonary artery occlusion to be evident on a chest film, the occlusion must involve a fairly large vessel, or there must be a sufficient number of small emboli to cause significant functional impairment of flow through the pulmonary vascular bed. If neither of these obtains, then, for identification on the chest film, there must be an infarct (necrosis of lung tissue) causing one or more localized parenchymal densities.

(2) *Pleural reaction or effusion* always indicates that infarction has occurred, though the parenchymal infarct may be hidden by the fluid. An infarct always

extends to the pleural surface, since the portion of a lung distal to the occlusion becomes necrotic because of lack of satisfactory collateral pulmonary circulation. Very rarely empyema or infected pleural effusion may occur.

(3) *Focal parenchymal densities* are described in some detail. The author considers "platter atelectasis" a common occurrence with pulmonary artery occlusion and a helpful sign in differentiating embolism or infarction from an infectious process. Theories explaining the development of the atelectasis are discussed.

The localization of the focal densities is of interest. Atelectatic changes (linear streaks) are usually seen at the bases. When they occur in the upper lung field, they tend to be more oblique, radiating upward and outward from the hilar areas. Frank infarcts are more commonly located in the right lower lobe. Six parenchymal radiographic patterns of pulmonary infarction are described: "vague infiltrate" or "pneumonitis" type, "nestler" (density nestling in the costophrenic angle with convex upper border), "wedge density," "lobar pneumonia type," "tumor type," and "edema type."

(4) *Pneumothorax* is listed as a rare manifestation of pulmonary infarct.

(5) *Changes in the peripheral vascular shadows* are believed to be associated with large vessel emboli. Spasm of the smaller pulmonary arteries probably has no roentgenographic manifestation that can be identified with routine technics.

(6) The problem of the patient with multiple small pulmonary emboli who develops gradually increasing dyspnea and possibly congestive heart failure is discussed at some length. The familiar finding of blanched peripheral lung fields with *abnormalities of the cardiac contour* is helpful in making this diagnosis. Changes in the cardiac contour in pulmonary embolism consist of either chronic or acute cor pulmonale. Difficulties in evaluating the degree of right ventricular enlargement and right atrial enlargement in the presence of other chamber enlargement are emphasized.

(7) Elevation of the diaphragm occurs frequently in pulmonary embolism alone, and even more frequently with infarction. The reason for this elevation in isolated embolism is unknown. In infarction it could be explained on the basis of splinting due to pleuritic pain.

This article is well illustrated by line drawings and roentgenograms.

RICHARD H. GREENSPAN, M.D.
University of Minnesota

An Early, Hitherto Unrecognized, Simple Roentgenographic Aid in the Diagnosis of Major Pulmonary Embolism. Louis A. Soloff and Jacob Zatuchni. Am. J. M. Sc. **237**: 608–611, May 1959. (Temple University School of Medicine, Philadelphia, Penna.)

The authors describe a new sign for the roentgenographic recognition of acute massive pulmonary embolism. This consists in an increase in the mid-right diameter of the cardiac silhouette. This diameter is the greatest horizontal distance between the mid-spinal line and the right border of the heart. In 50 randomly selected chest films of normal adults the mid-right diameter was 50 mm. or less in all but 3. An increase to greater than 50 mm. tends to be associated with an increased right atrial volume.

Unfortunately, the obtaining of comparable films on the same patient for measurement of the mid-right diameter would appear to be extremely difficult, since a chest film taken on a patient with acute pulmonary embolism is usually a portable film with a short focal-film distance, and is taken, as a rule, in the anteroposterior projection. A routine postero-anterior film at 6 feet certainly would give a different measurement. The case which the authors present exhibits this difficulty, with the pre- and post-infarct films not being of comparable technic.

[The idea behind the significance of this measurement appears to be sound, and one hopes that some standards for the mid-right diameter may be worked out, utilizing portable anteroposterior films rather than the routine 6-foot chest roentgenograms.—R. H. G.]

Two roentgenograms.

RICHARD H. GREENSPAN, M.D.
University of Minnesota

Agenesis in the Pulmonary Arterial Circulation. Report of Two Cases. George F. Lull, Jr., and Richard R. Taylor. Am. Rev. Tuberc. **79**: 641–651, May 1959. (Fitzsimons Army Hospital, Denver 8, Colo.)

Two cases of agenesis of a major part of the left pulmonary artery are presented. The authors suggest that this type of defect be grouped with those in which complete agenesis of one of the main branches of the pulmonary artery is present. The roentgenographic findings in these two patients were similar to those reported previously in patients with complete absence of a pulmonary artery. They consist of absence of the shadow of the hilus, increased radiolucency of the affected lung, decreased volume and decreased size of the thorax on the affected side, and herniation of the normal lung toward the involved side with an associated mediastinal shift in the same direction. This shift may make it impossible to be certain whether or not the major hilar vessels are present. There are a number of other conditions which may produce some of these signs so that, when the cause is not apparent, the authors believe that a combination of angiocardiography and bronchography is necessary to establish the diagnosis since the defect must be differentiated from absence of the pulmonary artery associated with agenesis of a lung.

Pulmonary function studies in the two reported patients, including bronchospirometry, showed a moderate decrease in ventilation on the involved side, with a rather marked decrease in oxygen consumption. This is similar to findings reported in patients with complete agenesis of the pulmonary artery. One of the patients had recurrent upper respiratory infections and moderate exertional dyspnea, while the chief complaint of the other was cough with hemoptysis and pleuritic pain. The authors regard these two symptoms of hemoptysis and chronic infection to be indications for surgical intervention. The hemoptysis supposedly is caused by hypertension in the pulmonary circulation as a result of the systemic circulation through aberrant arteries or through dilated bronchial arteries. Degenerative changes in the vessels as a result of the increased pressure must also be considered in this respect. Bronchiectasis has also been noted to be related to agenesis, and this further compromises the bronchial arteries and may cause hemoptysis. The increased frequency of infection is believed to be the result of structural changes in the bronchopulmonary tree

resulting in impaired drainage. The large volume of blood flowing into the abnormal lung through a dilated bronchial or aberrant artery places a strain on the left ventricle and may lead to heart failure. This event, along with frequent infections and hemoptysis, is a major indication for surgical resection.

Ten roentgenograms; 1 table.

JOHN H. JUHL, M.D.
University of Wisconsin

Surgical Considerations of Occlusive Disease of Innominate, Carotid, Subclavian, and Vertebral Arteries. Michael E. De Bakey, E. Stanley Crawford, Denton A. Cooley, and George C. Morris, Jr. Ann. Surg. **149:** 690–710, May 1959. (Baylor University College of Medicine, Houston, Texas)

Atherosclerotic occlusive lesions of the great vessels arising from the aortic arch and of the internal carotid arteries in the neck were well described by Broadbent many years ago (Tr. Clin. Soc., London **8:** 165, 1875). The recent advances in vascular surgery and angiographic technic have emphasized that many of these atherosclerotic lesions are segmental and surgically operable. The authors discuss in detail the pathology, clinical manifestations, and treatment of a series of 174 cases with manifestations of arterial insufficiency of the cerebrum and upper extremities. Of this group of patients, 73 (42 per cent) had extracranial occlusions; 63 of these were operated upon and 53 were found to have segmental disease susceptible to restorative surgery.

The occlusive lesions are of two main types: (1) proximal, involving one or more of the great vessels arising from the aortic arch; (2) distal, occurring near the origin of the internal carotid or vertebral arteries. The clinical manifestations depend upon the location and extent of the lesion. The proximal form produces arterial insufficiency of the cerebrum and upper extremities, while distal occlusion is manifested by cerebral arterial insufficiency alone.

The treatment and surgical technic are described. While the details are beyond the scope of this abstract, it may be pointed out that two types of procedure are used, namely endarterectomy and an end-to-side bypass with a suitable arterial graft.

Nineteen roentgenograms; 4 photographs; 16 diagrams; 4 tables.

J. S. ARAJ, M.D.
Toledo, Ohio

Clinical Uses of Functional Ascending Phlebography of the Lower Extremity. James A. DeWeese and Stanley M. Rogoff. Angiology **9:** 268–278, October 1958. (Strong Memorial Hospital, Rochester 20, N. Y.)

The authors describe their technic for functional ascending phlebography and analyze the results in 69 lower extremities of 54 patients in whom the procedure was performed.

Phlebography proved helpful in determining whether or not there was acute venous thrombosis in the lower extremities of 10 of 13 patients with either equivocal clinical signs of thrombosis or pulmonary emboli from an undetermined source. A definite phlebographic diagnosis of thrombosis should be made only if the defect has sharp margins in a heavily opacified vein; it must be visualized on at least two radiographs.

Phlebography was performed on 8 extremities of 7 patients with a clinical diagnosis of acute iliofemoral thrombosis. In all instances, complete obstructions of the iliac or common femoral veins were observed; these blocks were identified by lack of filling of these main veins and also by the appearance of numerous collaterals around the groin and pelvis. There was complete or almost complete obstruction of the superficial femoral and popliteal vein in 5 of the 8 extremities, but in only 3 of these was there extensive thrombosis with obstruction of the deep veins of the lower leg. The deep calf veins of the other 5 extremities were either normal or contained multiple bubble-shaped defects characteristic of thrombi. The great saphenous vein was well visualized in 5 of the extremities, emptying into significant collaterals in the pelvis. The consistent presence of obstruction of the common femoral and iliac vein and the less striking evidence of thrombosis in the distal veins in at least 5 of these extremities indicate that iliofemoral thrombosis probably originates in the iliac or femoral vein rather than in the lower leg. Post-thrombectomy phlebograms were obtained on 3 patients, 2 of whom had preoperative phlebograms for comparison. These comparative studies were useful in evaluating objectively a therapeutic procedure.

In 8 patients (10 extremities) with suggestive but not clear-cut histories of previous deep vein thrombosis, phlebography showed evidence of previous disease in only 1 extremity. The negative results were of equal value in the management of the patients.

Seventeen extremities of patients with complicated varicose problems but without historical evidence of previous deep venous thrombosis were examined. Valveless and/or abnormal dilated femoral veins were demonstrated in 8 of the extremities. These changes were unlike those observed in postphlebitic extremities. The failure of communicators, collaterals, and deep veins of the calf to empty after exercise was related to the presence of the abnormal femoral veins. The significance of these abnormal thigh veins and their contribution to venous stasis is discussed.

Phlebograms were obtained on 13 extremities of 11 patients with a history of chronic leg swelling for which there was more than one possible cause. Negative phlebograms strengthened the diagnosis of lymphedema in 6 patients and ruled out disease of the deep veins in 2 others. A diagnosis of old deep venous thrombosis was established in 2 patients.

Six figures; 3 tables.

A Modified Technique of Lower Limb Venography. R. Paton. Australian and New Zealand J. Surg. **28:** 312–315, May 1959. (Royal Perth Hospital, Perth, Australia)

The author describes a modification of previously described technics of "ascending venography" which will avoid necessity of a tourniquet and at the same time favor adequate filling of deep veins. The patient lies supine on the table with the feet tilted 10° downward. After appropriate antiseptic measures, a vein is selected on the medial side of the foot below the medial malleolus, a local anesthetic is injected, the vein is exposed, and a fine polyethylene tube inserted in a distal direction, as far as possible toward the sole of the foot. The system is flushed with isotonic saline solution, and an injection of 60 c.c. of 30 per cent Urografin is then given slowly over a period of about one minute. An anteroposterior roentgenogram is obtained, with the foot and leg in slight external rotation.

after injection is complete. The patient, who has been previously rehearsed, is then asked to perform the Valsalva maneuver for ten seconds and another exposure is made. Immediately following this, while the patient still is performing the Valsalva maneuver, another exposure is made of the popliteal region. A fourth film is exposed over the femoral and iliac regions about a minute later, with the patient relaxed.

Discussion and illustrations are presented to indicate that this technic is reliable and makes use of a tourniquet unnecessary. The Valsalva maneuver apparently aids in filling all the veins of the extremity and will force some of the contrast material into the subcutaneous system by reversal of flow along communicating veins whose valves are incompetent.

Five roentgenograms; 1 photograph.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

THE DIGESTIVE SYSTEM

The Radiologic Status of the Esophagogastric Segment: A Critical Review and Some Personal Observations. Christian V. Cimmino. Virginia M. Monthly **86**: 248–263, May 1959. (Mary Washington Hospital, Fredericksburg, Va.)

In this paper, the author discusses at length the esophagogastric section of the gastrointestinal tract.

In the *phrenic ampulla*, characteristic fluoroscopic findings, familiar to the radiologist, will serve for exclusion of hiatal hernia and esophageal reflux. Roentgenograms may show a soft-tissue shadow along the right border, merging into the diaphragmatic shadow. Often a shallow symmetrical groove may be seen in the ampulla, near its apex.

Various radiological appearances in the *vestibule*, or antrum, are described and grouped according to their significance. *Normally* there may be contraction of the entire vestibule immediately following a barium swallow, with minimal distention of the esophagus just above or the vestibule may be dilated while the adjacent esophagus is tonic. A tonic contraction of the vestibule with obstruction at the lower end of the esophagus may occur in apprehensive patients and in older persons. This also is classed as a normal finding, being related to emotional factors in the former group and to senescence in the latter.

A *borderline finding* is a lower esophageal contraction ring—a smooth, narrow, symmetrical encroachment upon the lumen best elicited during full inspiration. The fact that there is a higher incidence of esophageal diverticula associated with such rings than is explicable on the basis of chance suggests that they are not wholly innocuous.

Abnormal findings are persistent vestibular contraction, of which achalasia is the best example, and the occurrence of a constriction in the lower esophagus in hiatal hernia, with the cardial area above the diaphragm. This constriction ring is believed to represent the vestibular sphincter hypertrophied as a result of extra demands put upon it to prevent reflux.

In the *cardial region* there is convincing radiologic evidence of a valvular mechanism. The muscle tract said to form a cardial sphincter may be regarded as the agent for approximating the circumference of the cardial region so that the mucosal valve may operate.

The *phreno-esophageal membrane* is important in fixing the relative motion between the esophagus and diaphragm and is an antagonist to the longitudinal muscle of the former. With age its elastic and collagenous elements atrophy, predisposing to a sliding hiatal hernia.

The last of the anatomic elements to be considered in the esophagogastric segment is the *diaphragm*. The point is made that the esophageal hiatus is not a simple hole for passage of the esophagus. The thickened muscular rim has special functions. By its forces upon the lower esophagus it increases the angulation of the latter, which has been considered an important factor in esophageal continence. It serves also to help keep the cardial region in its proper place below the diaphragm. The hiatus usually becomes less snug with advancing age, and the radiographic boundaries between unusual laxity, hiatal insufficiency, and frank hernia are not sharp.

Recapitulating the constituents of the distal esophagogastric closing mechanism, the author states that the main component is probably at the cardial region. The causes for failure of the mechanism and the results of such failure are discussed. The most important cause is the sliding hernia. The results are esophagitis and ulceration. The latter is of two types: peptic erosion of the inflamed, edematous squamous mucosa of the esophagus and true peptic ulcer of gastric mucosa.

Hiatal hernias may be of the sliding or paraesophageal type, or mixed. When sliding hernia is suspected, the prime concern of the radiologist should be demonstration of reflux, for this is seldom demonstrated radiologically in the absence of hernia.

The clinical picture of paraesophageal hernia as opposed to sliding hernia with accompanying esophagitis, is dependent primarily on the space-occupying mass and may be dominated by cardiorespiratory or gastrointestinal complaints, including hemorrhage. Strangulation is an unusual occurrence and may defy radiologic demonstration.

The following radiologic classification of hernias depends primarily on the position of the cardial region.

A. Cardial incisura lost, and above diaphragm (sliding hernia): distal esophageal closing mechanism disturbed or lost; reflux present or imminent.

B. (1) Cardial incisura preserved: incisura below diaphragm (paraesophageal hernia); distal esophageal closing mechanism preserved; no reflux.

B. (2) Incisura above diaphragm (mixed hernia): reflux possible.

A bibliography of 67 references is appended.

Seventeen roentgenograms; 1 photograph; 1 diagram.

The Syndrome Pylorique: Clinical and Physiologic Observations. E. Clinton Texter, Jr., Hubbard W. Smith, William E. Bundesen, and Clifford J. Barborka, with the technical assistance of Junko Ikeya. Gastroenterology **36**: 573–579, May 1959. (Northwestern University Medical School, Chicago, Ill.)

"Syndrome pylorique" is a term used mainly in reference to ulcers of the pyloric ring. It has also been used in reference to benign pyloric hypertrophy in adults, benign pyloric tumors, and pseudoulcer distress. The authors describe the features of 67 cases of pyloric channel ulcer. Anatomically these ulcers are located in the pyloric canal, *i.e.*, between the prepyloric area of the stomach and the duodenum.

Pyloric channel ulcers account for 4.3 to 6.6 per cent of all peptic ulcers diagnosed radiographically. They occur predominantly in men (77 per cent), with the peak incidence in the fifth and sixth decades.

The major symptoms constituting the syndrome are pain, nausea, vomiting, and weight loss. The pain is rather atypical of ulcer: it may be colicky and unrelieved by eating, and it may require narcotics for relief. Nausea and vomiting were observed in 79 per cent of the patients and may occur immediately after eating or several hours later. Significant weight loss is frequent. Complications include complete pyloric obstruction and, less frequently, bleeding (17 to 34 per cent of cases). A single case of perforation has been reported.

The clinical course is usually rapid, the mean duration of symptoms being shorter than with gastric or duodenal ulcer. Weight loss is rapid, and pyloric obstruction occurs early. Medical treatment is not very satisfactory. Eleven of the authors' cases responded to intensive medical therapy, while 30 had gastric surgery.

The roentgen diagnosis of channel ulcer is difficult. Careful study is required to demonstrate the pyloric channel and an ulcer niche in this area. Other signs are tortuosity and straightening of the canal and slowed antral evacuation.

Physiologically, patients with pyloric channel ulcer tend to have high secretory volumes—due to gastric retention—with a low level of gastric acidity. Dysfunction of the antral evacuation mechanism has been demonstrated by measurements of intraluminal pressures and inability to pass a catheter through the pylorus into the duodenum. Several patients were studied fluoroscopically, and in these it was possible to correlate the presence of pain with peristaltic waves traveling down to the pylorus without producing gastric evacuation. Abnormalities of motor function account for the major symptoms comprising the syndrome pylorique.

The incidence of cancer originating in the pyloric channel appears to be extremely low. There was no evidence of malignant change in the 67 cases presented. Thirty of the cases were found to be benign at surgery, and 37 have had long term follow-up.

Three roentgenograms; 2 diagrams.

CAPT. ALLAN E. GREEN, JR., M.C.
Lackland AFB, Texas

Current Status of the Early Diagnosis of Gastric Carcinoma. E. Hafter. Schweiz. med. Wchnschr. **89:** 15–20, Jan. 3, 1959. (Tödistrasse 36, Zurich, Switzerland)

Procedures to find gastric carcinoma in its early stages and the reasons for late diagnosis are described. Early discovery is possible in most cases if the patient is sent to the roentgenologist for careful examination. Gastroscopy and radiography are the most useful diagnostic methods.

Early cancer of the stomach may show any of three forms, either singly or in combination: it may be infiltrating with rigidity of the stomach wall; tumorous with filling defect; or ulcerative, with a niche.

Four cases are reported in detail. In the first, roentgen studies seven and again four years before death missed the diagnosis although at the second examination a niche the size of a hazel nut was found in the angle of the stomach with a small, unrecognized bulbar filling defect. Three months before death, a roentgen diagnosis was confirmed at laparotomy, when metastases were also found. The second, third, and fourth patients had lived, at the time of this report, two years, four years, and three years, respectively, without recurrence after resection. Case II was an ulcerous carcinoma of three years duration, so strongly suspected roentgenologically that despite a negative test, resection was performed and the diagnosis established. In the third case there was a five-year history of an ulcerous infiltrating cancer. Case IV had shown for twenty years the characteristic symptoms of a hiatal hernia when, four months before surgery, pain, gastric hemorrhage, a hemoglobin fall to 50 per cent, and roentgen studies led to the diagnosis of carcinoma.

Eight roentgenograms; 4 diagrams; 1 table.

Carcinoma at the Margin of the Gastrojejunostomy Stoma. Review of the Literature and Report of a Case. Alan R. Aronson and Donald R. Darling. Gastroenterology **36:** 686–690, May 1959. (University of Illinois, Chicago 12, Ill.)

A case of carcinoma developing at the gastroenterostomy stoma is reported and discussed in conjunction with a review of 19 cases from the literature.

The authors' patient was a 70-year-old Caucasian male who underwent a posterior gastrojejunostomy in 1933 for duodenal ulcer symptoms. He remained well until April 1957, when ulcer-like symptoms recurred. Roentgen examination showed a well functioning gastroenterostomy without evidence of ulcer. A filling deformity of the greater curvature in the region of the antrum was attributed to previous surgery. [Exact relationship-in-time of this examination and subsequent autopsy is not given.] The patient's condition gradually deteriorated, pulmonary edema ensued, and death occurred in October 1957. Autopsy demonstrated "carcinoma simplex of the stomach involving the margin of the gastrojejunostomy and infiltrating into the surrounding tissue."

The average age of onset of gastric carcinoma at the gastroenterostomy site in the 20 collected cases is fifty-eight years. This approximates the average age of onset of carcinoma in the intact stomach. Average duration following surgery to the appearance of symptoms is eighteen years. In only 2 patients were the gastroenterostomies not functioning on x-ray evaluation; the remaining stomas were considered normal roentgenologically. Gastroscopic examination is recommended as the definitive diagnostic procedure.

One roentgenogram; 1 table.

MAJ. WILLIAM H. ELLSWOOD, M.C.
Lackland AFB, Texas

Carcinoma of the Stomach Appearing After Previous Gastric Surgery for Benign Ulcer Disease. Donald Berkowitz, Paul Cooney, and S. Philip Bralow. Gastroenterology **36:** 691–697, May 1959. (101 South 20th St., Philadelphia 3, Penna.)

The authors cite 8 cases of gastric cancer following surgery for benign ulcer. The average age of the patients was sixty-two years; the average interval between the original operation and the diagnosis of cancer was twenty-one years. The presenting symptoms were of three main types: those of advanced malignant disease, those simulating the postgastrectomy syndrome, and those of recurrent ulceration. Gastroscopy (performed in 5 cases) is diagnostic in 60 per cent and roentgenology in 38 per cent of the cases. Three cases were misinterpreted roentgenologically as stomal ulcers, 1 as a defect secondary to previous surgery and 1 was called an antral gastritis.

Other authors have reported 5 and 11 per cent

incidence of gastric cancer in patients with previous gastric surgery for benign disease. The type of operation appears to have no influence on the incidence of the development of cancer. In the group operated for gastric ulcer the frequency of subsequent malignant disease was three times the expected rate, while in the duodenal ulcer group the observed and expected frequencies were essentially the same.

The authors recommend x-ray study soon after gastric surgery to serve as a baseline record for comparative studies in the future.

Six roentgenograms; 1 photograph; 1 table.

CAPT. SAMUEL S. KRIKORIAN, M.C.
Lackland AFB, Texas

Chronic Myelogenous Leukemia with Gastric Infiltration. Report of a Case Simulating Carcinoma of the Stomach. John A. Cavins, Hugh S. Levin, and H. James Day. New England J. Med. **260:** 1111–1114, May 28, 1959. (Ohio State University Health Center, Columbus, Ohio)

Lymphomatous invasion of the stomach occurs most frequently in Hodgkin's disease, lymphosarcoma, and chronic lymphatic leukemia. Gastric infiltration in chronic myelogenous leukemia is rare. The authors describe a case of this unusual type.

The patient sought medical care because of gastric symptoms. Clinical and radiologic evidence indicated a diagnosis of gastric carcinoma. Hematologic examination revealed chronic myelogenous leukemia but because of the rarity of infiltration of the stomach in that condition an associated carcinoma was assumed. At laparotomy the appearance was that of carcinoma, but microscopic study revealed a localized infiltration of leukemic cells into the stomach wall and led to a diagnosis of myelogenous leukemia.

Following operation, the patient experienced complete symptomatic relief. This suggests that all patients with leukemia and gastric complaints should have thorough radiologic, gastroscopic, and biopsy examinations, since surgical relief is possible.

One roentgenogram; 2 photomicrographs; 1 table.

JOHN F. RIESSER, M.D.
Springfield, Ohio

The Importance of Preoperative Roentgen Diagnosis of Anomalies of Intestinal Rotation. Kurt H. Kent and Harvey J. Raszkowski. Gastroenterology **36:** 633–641, May 1959. (St. Francis Hospital, Lynwood, Calif.)

The principal errors of intestinal rotation, though usually obvious on roentgenograms of the upper gastrointestinal tract, are frequently overlooked and omitted from the routine radiographic report. Basic embryologic errors of intestinal rotation are: (1) nonrotation (common mesentery); (2) partial rotation (malrotation); (3) failure of cecal descent (mobile cecum, subhepatic cecum). Innumerable variations of these three main types are possible, depending upon the degree of mesenteric fixation. The most significant errors involve the midgut, *i.e.*, the segment of the alimentary tract between the second portion of the duodenum and the mid transverse colon, which receives its blood supply from the superior mesenteric artery. Abnormalities in the mesentery predispose to complications such as volvulus and obstruction by bands. Complications may occur at any time in life, or the anomaly may remain completely asymptomatic.

Advance knowledge of anomalies of rotation is of great importance in the event of an acute abdominal emergency. Two cases are presented in which such knowledge aided the surgeon in the diagnosis of acute abdominal crises and simplified surgery by providing an exact knowledge of the abnormal anatomy.

Roentgen diagnosis of common mesentery and incomplete rotation is simple. The normal closed duodenal C-loop is absent or is replaced by an "open loop." The third portion of the duodenum fails to cross over the spine to the left side of the abdomen. The jejunum is on the right side of the abdomen but may, if its mesentery is long enough, swing from side to side. A barium enema will indicate the extent of failure of rotation.

Seven roentgenograms.

CAPT. JOHN R. BROADWATER, M.C.
Lackland AFB, Texas

Jejunal Adenoma Producing Intussusception—Report on a Case. J. Colquhoun. Brit. J. Radiol. **32:** 329–331, May 1959. (Addenbrooke's Hospital, Cambridge, England)

The authors describe a case of adenomatous polyp of the jejunum which produced intussusception. Symptoms had been present for six years before the diagnosis was made by radiologic examination. Repeated transfusions had been given for melena. An upper gastrointestinal examination disclosed a filling defect in the upper portion of the jejunum. Several inches distal to this, the jejunum was dilated. One half-hour later, fluoroscopy showed a round tumor leading an intussusception. Palpation of the abdomen resulted in unintentional reduction of the intussusception. An hour after this, a well-formed intussusception was demonstrated. At operation a finely nodular gray mass 2 cm. in diameter, with attached stalk, was removed and microscopically was found to be a benign adenomatous polyp.

Benign small bowel tumors have no distinct clinical features. The onset of symptoms may be insidious and mimic other conditions, particularly duodenal ulcer. The commonest manifestations are those of acute or chronic intestinal obstruction and melena without obvious cause in the upper or lower gastrointestinal tract.

This case illustrates the necessity for careful examination of the small intestine when routine procedures fail to reveal the cause of melena.

Four roentgenograms.

THEODORE E. KEATS, M.D.
University of Missouri

Carcinoma and Ulcerative Colitis; A Clinical-Pathologic Study. III. Survivors. Moshe B. Goldgraber, Eleanor M. Humphreys, Joseph B. Kirsner, and Walter L. Palmer. Gastroenterology **36:** 613–630, May 1959. (950 East 59th St., Chicago 35, Ill.)

Nine cases of cancer of the large bowel occurring in patients with ulcerative colitis are described. The patients in this selected group were all alive at the time of the report and under observation. Case histories with clinical, surgical, and pathological findings are presented.

The age range at the time of diagnosis of a neoplasm was from nineteen to sixty-eight years The average duration of ulcerative colitis symptoms before the tumor was diagnosed was 11.2 years. The distribution

of the tumors over the colon was more even than is usual in cancer of the colon. One case was primary in the appendix. Pseudopolyps were seen in 7 cases. Multiple carcinoma occurred in 4 cases. Node involvement was present in 2 patients who had survived two and eight years, respectively.

Fifteen photomicrographs; 1 table.

CAPT. HARRIS W. KNUDSON, M.C.
Lackland AFB, Texas

Perforation of the Rectum or Colon in Infancy Due to Enema. Thomas V. Santulli. Pediatrics **23:** 972–976, May 1959. (Babies Hospital, New York 32, N. Y.)

Nine cases of perforation of the rectum or colon in infancy, due to an enema, are reported from the Babies Hospital, New York, to call attention to the inherent dangers of a common procedure, which is usually regarded as simple and innocuous. A cleansing enema was the cause or inciting factor in 4 cases. In 4 others, a diagnostic enema study (barium in 2 and Hypaque sodium in 2) was responsible. In the ninth case perforation was produced by a catheter used to rupture a congenital anal membrane. Six of the children succumbed; 3 survived.

The mechanism of perforation and the factors contributing to the complication are discussed. In the author's opinion, it is unlikely that intraluminal pressure alone is responsible for perforation of the normal bowel during a barium enema examination or during the usual cleansing enema administered by gravity pressure. Emphasis has been properly placed on the danger of over-distention of a balloon of the rectal catheter at the rectosigmoid level where the intestine is relatively fixed by the peritoneal reflection. This is probably the mechanism of rupture during the performance of a diagnostic barium enema examination. In other cases, actual perforation of the wall of the bowel by a catheter or enema tip must be regarded as the direct cause. The relatively small size of the bowel and the short distance from anus to rectosigmoid area are important factors in the mechanism of perforation in infants, particularly since the patient is often uncooperative and struggling.

In reviewing the technic of administration of the enema or passage of the rectal tube in the cases of perforation reported here, several factors were disclosed. In some infants the catheter or its attached balloon was too large or the tube was introduced too far into the rectum. In other cases, persistence in trying to fill the entire colon when it was unnecessary in relation to the information sought and the inability to control movements of the patient (and catheter) during fluoroscopic visualization in the dark room were important factors contributing to the accident.

Five roentgenograms; 1 table.

Routine Cholangiography During Operation for Gallstones. C. C. Smith and George A. Faris. California Med. **90:** 332–334, May 1959. (Santa Clara County Hospital, San Jose 12, Calif.)

In 1955 and 1956 the authors began routinely to obtain cholangiograms during operation for gallstones. A mobile x-ray unit rated at 100 ma at 100 kvp makes practical exposures at a fraction of a second. Technical factors are 90 kvp, 100 ma, 0.3 second, 2-mm. Al filter, a 5-inch cone to limit the field to a 10-inch circle, and 40-inch tube distance. The film is processed immediately and if its appearance suggests a stone in the duct, another exposure is made after irrigation and reinjection of contrast medium.

If at operation the common duct is obviously inflamed or contains palpable stones it is usually opened at once and the cholangiogram obtained later by introducing the medium through the T tube left in place. If the gallbladder has been removed, the injection of Hypaque is made through a needle inserted into the common duct.

Six case reports are given, illustrating the value of the procedure in various situations.

Six roentgenograms.

THE MUSCULOSKELETAL SYSTEM

(Including Tumors in Spinal Canal)

Arteriography in Bone Diseases. Eduardo Girão do Amaral. Gaz. méd. port. **11:** 419–453, July-August; 567–627, September-October; 699–712, November-December 1958. (In Portuguese) (Faculdade de Medicina, Lisbon, Portugal)

This is a monographic contribution to the diagnostic significance of arteriography in bone diseases. The paper appears in three installments, of which the third contains only technical details. It is based on findings in 271 patients with bone disease (seen in the Surgical Service of Prof. Cid dos Santos), all of whom had been subjected to arteriography.

The first installment begins with a general introduction, a brief historical sketch, an account of "normal" arteriographic aspects, followed by a description of the findings encountered in 26 cases of fracture (including 1 of the femoral shaft caused by Paget's disease), in 72 cases of nonspecific osteomyelitis, in 1 case of osseous tuberculosis, in 25 cases of osteo-articular tuberculosis, in 17 cases of bone syphilis, and in 5 cases of solitary bone cysts (2 of which had caused femoral shaft fractures). In these diseases, arteriography does not provide characteristic patterns. The information will be at best negative. Nonvisualization of the vascular tree within the bone structure speaks for a benign condition.

The second installment is devoted to bone tumors, beginning with 7 cases of osteochondroma and 1 case of chondroma. These are also benign and thus exhibit nonspecific appearances. On the contrary, 39 instances of osteogenic sarcoma, 41 of unclassified sarcoma and metastases, 3 of Ewing's tumor, and 9 of multiple myeloma (including 1 with pathologic fracture) showed typical vascularization patterns within the tumor. Often, pooling can be seen, forming so-called "venous lakes." It seems that arteriography permits the determination of the actual extent of the malignant process in bones. In the author's experience, this characteristic appearance would fade in radiosensitive tumors following therapy. He believes that increased vascularity within the tumor is due to higher metabolic needs of malignant tissue. [Since Warburg's experimental proof, it is generally accepted that tumor cells consume no more, and sometimes less, oxygen than "normal" cells. Increase in blood supply for tumor tissue is necessitated by the increase in total number of cells.—E. R. N. G.]

Arteriography was also performed in 13 patients with benign giant-cell tumor. In the latter disease, the appearance is peculiar, inasmuch as the contrast

medium produces homogeneous opacification of the tumor but vessels reach only to its periphery (which serves as a means of arteriographic differentiation from a malignant neoplasm). The "venous lakes" are absent in benign giant-cell tumors.

The author states that a fourth installment—to be published at a later date—will take up the arteriographic aspects of Paget's disease, Albers-Schönberg's osteopetrosis, intraosseous hematoma of hemophilic origin, calcified hematoma, and fibrous dysplasia.

Valuable bibliographies are included.

One hundred five figures. E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

The Diagnostic Usefulness of Skeletal Maturation in an Endocrine Clinic. William J. Mellman, Alfred M. Bongiovanni, and John W. Hope. Pediatrics **23:** 530-544, March 1959. (J. W. H., 1740 Bainbridge St., Philadelphia 46, Penna.)

The findings in 146 children referred to an endocrine clinic have been analyzed, with particular attention to the diagnostic significance of bone age in endocrine problems. The clinical records of the children were reexamined and the bone ages, estimated from the time of appearance and fusion of several centers of ossification, were determined from roentgenograms made at the time of referral, by the same person, using mean standards adopted from the compilations of Stuart and Stevenson (Textbook of Pediatrics, 1954) and Maresh (In Boyd, E.: An Introduction to Human Biology and Anatomy, 1952). The height age, from averages of Engelbach, as tabulated by Wilkins (Diagnosis and Treatment of Endocrine Disorders of Childhood and Adolescence, 1957), was recorded for each individual studied. The entire group was separated into two sections: (1) those who showed physical retardation in terms of linear growth or epiphyseal ossification; (2) those who were physically advanced on the same basis.

Ninety-five children were retarded with respect to height, bone age, or both. Only 30 per cent of this group had a true endocrinologic disorder; in the majority this was hypothyroidism. Retardation of skeletal maturation alone, however, is not indicative of thyroid disease. The majority of the children with retardation had a "constitutional" disorder.

Fifty-one children exhibited acceleration of the bone age, stature, or both. In 20 it could be attributed to constitutional precocity. Such advancement, of a moderate degree, was associated with simple exogenous obesity. The most extreme alterations were seen in conjunction with adrenal hyperplasia or adenoma.

The importance of employing several centers for the estimation of bone age is stressed, and the significant diversity which may occur between the hand and wrist and other regions is detailed in several instances. A summary of concepts relating the endocrine system to maturation, in terms of the clinical data described, is presented.

Twelve graphs; 10 tables.

Roentgenologic and Clinical Aspects of Multiple Myeloma with Report of an Unusual Case. Otto Deutschberger and Herley Fujiy. Ann. Int. Med. **50:** 1309-1320, May 1959. (27 W. 86th St., New York 24)

The roentgenologic features of multiple myeloma have been found not to be characteristic. The well defined, punched-out destructive lesions so frequently described are actually rather exceptional. Bone findings on radiologic examination range from normal through phases of osteoporosis and osteolysis to severe widespread bone destruction. The authors attempt to show that these findings may vary not only from case to case but even within the same individual. They explain these various manifestations on the basis of stage of the disease, rapidity of its progression, and attempts of the host to limit its spread. Several radiologic appearances can be present in the same person at the same time.

This "radiologic multiformity of multiple myeloma" is illustrated by a case report. The case is unusual also for its atypical clinical features. The patient was a 24-year-old female with relatively little pain and without severe anemia, Bence-Jones protein, hypercalcemia, or increased serum globulin, in spite of widespread skeletal involvement with extensive bone destruction. Roentgenograms demonstrated (1) punched-out, round areas of rarefaction without bone repair, widely disseminated through the skeleton in "textbook" fashion, (2) osteoporosis of the spine, and (3) compression fracture of the second lumbar vertebra.

Six roentgenograms; 1 photomicrograph; 4 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

The Treatment of Parosteal Osteoma of Bone. Murray M. Copeland and Charles F. Geschickter. Surg., Gynec. & Obst. **108:** 537-548, May 1959. (Georgetown University Medical Center, Washington, D. C.)

The authors present 22 cases of parosteal osteoma of which 16 were previously reported (Ann. Surg. **133:** 790, 1951. Abst. in Radiology **58:** 776, 1952). The tumor occurs in both benign and malignant forms, with the malignant form predominating. It is seen most often in the first four decades of life and principally on the posterior surface of the lower femur. On roentgen examination, a mass 5 to 10 cm. in diameter, densely ossified, circumscribed, frequently sharply outlined, occurring outside the bone but contiguous to it, is usually visible. To be differentiated are localized myositis ossificans, intraligamentous osteoma, sclerosing osteogenic sarcoma, and osteochondroma.

A review of the authors' series emphasizes the fact that parosteal osteomas are potentially malignant. Of the 22 cases, 14 originally appeared to be benign. Altogether, however, the tissue removed either at the original or a subsequent operation was considered malignant in 15 patients, benign but cellular in 3 specimens, and typically benign in only 4. Of 18 patients for whom determinate results were available, 11 were living and well five or more years following resection or amputation. The absolute five-year survival rate was 63.6 per cent; the adjusted, for the patients treated, was 60 per cent.

The best results are obtained by bold, early ablative surgery—resection or amputation.

Ten roentgenograms; 12 photomicrographs; 1 photograph; 1 diagram; 1 chart; 1 table.

JOSEPH M. WINSTON, M.D.
University of Pennsylvania

Some Radiological Aspects of Congenital Anomalies of the Spine in Childhood and Infancy. John Fawcitt. Proc. Roy. Soc. Med. **52:** 331-333, May 1959. (Manchester, England)

Coronal Cleft Vertebrae: In the later stages of pregnancy views showing the fetal spine in lateral projection

may demonstrate one or several lumbar or dorsal vertebrae with a vertical translucent cleft situated slightly more posteriorly than anteriorly. The affected vertebrae tend to appear somewhat larger than the adjacent normal ones. The author encountered 7 such cases in eighteen months. Four were discovered on films of the fetus and 2 were visible in lateral radiographs made at the time of delivery. The remaining case was discovered incidentally in an infant of three weeks with an acute respiratory infection. Males outnumbered females 5 to 2. In 2 cases the cleft disappeared, as shown by films made a few weeks to a few months later. It is concluded that the finding is an anatomical variant in ossification and does not carry pathological significance.

Spina Bifida: The author reviewed 500 consecutive unselected lumbar spine radiographs of children and in 82 per cent found some element of spina bifida occulta (defined as incomplete closure by ossification of the laminae of any of the vertebrae included on the radiographed segment). When the cases were divided into three groups—from birth to five years, six to ten years, and eleven to sixteen years—some degree of spina bifida was found in 94 per cent of the children examined in the first quinquennium, with the percentage falling to 74 and 75 per cent in the later age groups. This is explained by the fact that completion of ossification of the posterior processes occurs during the first five years of life.

In more than one-half of the cases the anomaly was found at the first sacral segment; in almost three-fourths at either L-5 or S-1.

It is concluded that "spina bifida in childhood ought not to pass unreported by the radiologist, particularly in cases of congenital anomalies of the lower limbs." Diastematomyelia is occasionally associated and must not be overlooked

Three roentgenograms; 1 table.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Observations on Spinal Tumours in Childhood. Kenneth Till. Proc. Roy. Soc. Med. **52:** 333–336, May 1959. (Hospital for Sick Children, London, England)

During a five-year period from 1953 to 1958, only 28 children in 1,300 admissions to the Department of Neurosurgery at the Hospital for Sick Children (London) had spinal canal tumors. Neuroblastoma accounted for 7 cases and "arachnoid cysts" for 3. The rest were assorted tumors of wide variety.

In diagnosis, two principal difficulties peculiar to this age group are encountered: *pain* is infrequent and testing for *sensory loss* is often unreliable.

Three cases are briefly presented to demonstrate the problems of accurate diagnosis and to show how a tumor can grow to a considerable size in a child's spinal canal, producing long-standing but minimal symptoms, without in any way provoking prominent neural dysfunction or abnormal neurologic signs. A plea is made for more frequent use of contrast myelography and studies of cerebrospinal fluid in children presenting with vague symptoms referable to the spine or neural system when other explanations are not forthcoming. One of the cases is of particular interest because of a congenital anomaly (diastematomyelia) occurring with an intraspinal tumor subsequently proved to be a hamartoma.

The importance of careful study of plain roentgenograms of the spine is stressed. Such study must include close scrutiny of pedicles, measurement of interpedicular distances and intervertebral foramina, recognition of erosion or absorption of posterior borders of vertebral bodies, and the presence of abnormal calcification or bony pegs and spurs.

Three roentgenograms; 1 table.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Coxa Protrusa: Contribution to the Radiologic Study of Some Malformations of the Hip. Gianluigi Buraggi. Radiol. med., Milan **44:** 958–971, October 1958. (In Italian) (Istituto di Radiologia dell' Università di Milano, Italy)

The developmental abnormalities of the acetabular cavity range from complete absence (acetabular aplasia with congenital dislocation of the hip), through shallow, average, and deep acetabula, to protrusion of the femoral head into the pelvis. This last condition was first described in 1824 by A. W. Otto [Otto pelvis].

Such a "coxal protrusion" is not necessarily of developmental origin. It may appear as a result of trauma ("central femoral luxation"), in association with benign or malignant neoplasms, or after other diseases which cause softening of the bones (localized infections, as specific or nonspecific osteomyelitis, or metabolic changes such as osteomalacia or rickets). When the patient is first seen in a late stage of the disease, the overlay of degenerative changes may be so heavy as to obscure the original etiology. Under these circumstances, adequate diagnostic evaluation will require correlation with the clinical history.

Ten roentgenograms; 11 diagrams.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Slipping Epiphysis of the Hip: A Roentgenological and Clinical Study Based on a New Roentgen Technique. Lars Billing and Erik Severin. Acta radiol. Suppl. 174, 1959. (University of Gothenburg, Sweden)

The authors made a study of 63 patients with slipping femoral epiphyses in one or both hips, using a method of roentgenologic measurement which Billing first described in greater detail in 1954 (Acta radiol. Suppl. 110. Abst. in Radiology **65:** 140, 1955). The method, analysis of findings, treatment, and results defy brief abstracting. The paper deserves reading in its entirety by those interested in this problem.

An interesting, and perhaps debatable, finding was an incidence of 80 per cent bilateral slippage.

A short section on traumatic epiphysiolysis is included.

Eighty-one roentgenograms; 5 photographs; 14 diagrams and charts. HOWARD J. BARNHARD, M.D.
Hahnemann Medical College, Philadelphia

Fatigue Fracture of the Pelvis and the Lower Extremity. C. C. Wang, C. W. Lowrey, and R. L. Severance. New England J. Med. **260:** 958–962, May 7, 1959. (R. L. S., Fort Chaffee, Ark.)

Fatigue fracture, or march fracture, is a condition most commonly found in healthy recruits who are suddenly subjected to physical training. The present paper is based on 97 fractures found in 83 patients. Seventy-five of the fractures were in the metatarsal bones while the others involved the pelvis, femur so

calcis, and tibia. The fractures were generally ushered in by a constant dull, aching pain in the involved bone, promptly relieved by nonweight bearing.

Two patients had bilateral pelvic fractures at the junction of the pubic and ischial bones. In the femur (3 patients), the location was the lower third, about 15 cm. proximal to the knee. The tibial fractures (8 patients) were all in the upper third, approximately 12 cm. distal to the joint. The fractures of the os calcis (4 patients) were in the posterior portion of the bone. Almost all of the 75 metatarsal fractures (66 patients) involved either the second or third metatarsals at the junction of the middle and distal thirds.

The fracture line may defy detection or in some instances may be seen as a faint transverse radiolucency extending in from the cortex of the involved bone. With healing there is periosteal reaction, often extending for a considerable distance up and down the shaft of the femur or tibia. Metatarsal fractures tend to heal with abundant callus. An irregular sclerotic zone within a bone transverse to the long axis may be found and is said to be diagnostic of fatigue fracture. This is particularly characteristic of the fractures of the os calcis, where there is little periosteal reaction or callus during the healing phase.

It cannot be overemphasized that in some cases of early fatigue fracture radiographic findings may not be sufficiently developed to be recognized. It is therefore extremely important to re-examine the involved parts two or three weeks after the initial procedure if a fatigue fracture is seriously considered.

Treatment is rest for ten days followed by gradual ambulation, with full activity possible in six to eight weeks.

Ten roentgenograms.

MAJ. MARTIN A. THOMAS, M.C.
MacDill AFB, Fla.

Multiple Ossification Centres in the Epiphyses of the Long Bones of the Human Hand and Foot. A. F. Roche and S. Sunderland. J. Bone & Joint Surg. **41-B:** 375–383, May 1959. (University of Melbourne, Melbourne, Australia)

This paper directs attention to the frequency of multiple ossification centers in the epiphyses of the long bones of the hands and feet. The authors made serial radiological examinations of the hands and feet of a group of 60 boys and 60 girls, all normal and healthy. The children were examined at three-monthly intervals from the age of two to four years. The findings were as follows:

In the hands of the boys, only the epiphysis of the first proximal phalanx showed multiple centers more often than single ones, but among the girls, multiple centers did not appear more often than single ones in any epiphysis.

Both in the boys and in the girls, multiple ossification centers were more common than single ones in the first metatarsal and in the first, second, and third proximal phalanges of the foot. This high incidence of multiple centers of ossification in the epiphyses of the first metatarsal and proximal phalanx of both hands and feet in both sexes suggests that this should be regarded as the normal pattern of ossification.

Multiple centers of ossification occurred simultaneously in several epiphyses of the same hand or foot. They were always circumscribed and later showed trabeculae. In many of the children, they eventually fused to form an epiphysis of conventional appearance and shape.

It was noted that there seems to be a relationship between the shape of an epiphyseal area and the pattern of ossification occurring within it.

Care should be taken to avoid confusing these normal patterns of ossification with radiological appearances resulting from pathological changes.

Sixteen roentgenograms; 4 tables.

RAUF YAGAN, M.D.
Cleveland Metropolitan General Hospital

A Case of Congenital Arteriovenous Aneurysm Involving the Femur. R. C. Howard. J. Bone & Joint Surg. **41-B:** 358–361, May 1959. (9 Town Close Road, Norwich, England)

A case of congenital arteriovenous aneurysm involving the femur is presented, in which the definite diagnosis was made at surgery by auscultation of the involved area. The strange cavernous rumblings of an arteriovenous aneurysm involving the bone were heard with the stethoscope. There was also a pronounced apical systolic murmur. The changes on the routine radiographs could not be differentiated from monostotic fibrous dysplasia.

After operation, a femoral arteriogram was obtained, showing multiple ramifications of the arteriovenous anastomosis involving the femoral artery and vein. Following ligation of the anastomosing fistulae at a second operation, the systolic murmur disappeared, and about four years after surgery the radiological appearance of the femur was normal.

From this experience, the author considers that auscultation of suspected bone tumors should be considered an important part of the routine clinical examination.

Three roentgenograms; 2 tracings.

RAUF YAGAN M.D.
Cleveland Metropolitan General Hospital

Monosteotic Fibrous Dysplasia of Radius. C. S. V. Subramanyam. Indian J. Radiol. **13:** 63–70, May 1959. (Armed Forces Medical College, Poona, India)

A 32-year-old male gave a ten-year history of gradual enlargement of the forearm. Roentgenograms revealed a fusiform multicystic area of translucency replacing the radius except in its distal portion. Surgical resection of this "tumor" was successful, without physical disability to the patient. Histologic sections were consistent with fibrous dysplasia. The interesting features of the case are the long history, size of the mass (770 gm.), and success of the surgical procedure.

Three roentgenograms; 3 photomicrographs; 2 photographs.

J. S. ARAJ, M.D.
Toledo, Ohio

GYNECOLOGY AND OBSTETRICS

Diagnostic Possibilities of Amniography. A. Tetti and A. Barbanti. Radiol. med., Milan **44:** 929–938, October 1958. (In Italian) Università di Torino, Turin, Italy)

Amniography as used by the authors consists in transparietal puncture of the amniotic sac, aspiration of 50 c.c. of amniotic fluid, and injection of 20 to 40 c.c. of an organic iodinated medium. A satisfactory positive outline of the uterine cavity is obtained, with negative contrast of the fetal parts. The method

affords (1) visualization of placental insertion site, (2) proof of presence or absence of uterine malformations (bicornuate uterus) or other abnormalities (protruding fibroids, other masses), (3) in case of multiple pregnancies, assessment of the mono- or poly-amniotic situation, (4) determination of fetal sex (may require special positioning to visualize the scrotal sac), (5) information as to fetal malformations, (6) confirmation of fetal death, (7) confirmation of rupture of fetal membranes ("transvasation"), (8) demonstration of painless uterine contractions, (9) evaluation in "overdue" cases, and (10) urographic study (contrast medium eliminated *via* maternal kidneys).

In the authors' cases, neither mother nor fetus suffered any untoward results which could be ascribed to this amniographic procedure.

Five roentgenograms. E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

X-Ray Pelvimetry. Edward A. Graber, Hugh R. K. Barber, and James J. O'Rourke. Am. J. Obst. & Gynec. **77:** 28–33, January 1959. (Lenox Hill Hospital, New York 21, N. Y.)

Two hundred and forty-two cases in which x-ray pelvimetry was employed have been reviewed with the purpose of evaluating the accuracy and usefulness of the procedure. The methods of roentgen evaluation utilized were those of Thoms, Ball, Snow, Colcher and Sussman, and Caldwell and Moloy. The examinations were reported by 18 different radiologists.

The x-ray prognosis was correct in 3 out of 4 cases, but the great majority of these reports dealt with a normal or almost normal pelvis and a baby of average size. The highest incidence of error was in the borderline situation. Inability of the radiologist to judge the size of the fetal head accounted for the largest number of errors, regardless of the method used. Thus, according to the authors, x-ray examination offers no real help where the obstetrician needs it most—in cases of cephalopelvic disproportion, due either to the borderline pelvis or to the unsuspected larger fetus in the average pelvis.

It is suggested that the radiologist does not usually have sufficient information or the obstetrical background to make a clinical prognosis and should cease predicting the outcome of delivery, since by his prediction he places the obstetrician in an untenable position medicolegally.

X-ray pelvimetry was never intended to take the place of an adequate pelvic examination and trial of labor. It is a laboratory aid at best and should be used as such. The authors believe that it should be limited to two situations: (1) malpresentation and (2) lack of adequate clinical progress in labor. For maximum information, roentgen examination should be made only while the patient is in labor. Because of the danger from excessive radiation, the obstetrician should specify the number of views to be taken for the individual case.

Five tables.

Radiation Reduction in Diagnostic Obstetrical Radiography: The Application of Electronic Photographic Techniques. R. M. Lowman, E. Donnellan, and S Goldenthal. Am. J. Obst. & Gynec. **77:** 18–27, January 1959. (Grace-New Haven Community Hospital, New Haven, Conn.)

The addition of LogEtronic processing of underexposed pelvimetry roentgenograms reduced the radiation to the fetal and maternal pelvis. Electronic revision of poorly exposed films occasionally reduced the necessity for re-examinations and obviated the additional radiation exposure. This technic was combined with certain physical factors known to reduce radiation exposure: (1) increased aluminum filtration or use of a brass wedge; (2) high-speed screens; (3) high-kilovoltage; (4) high-speed film emulsions; (5) improved developing technic. On the anteroposterior view of the abdomen, the underexposure technic resulted in 60 per cent and on the lateral view in 40 per cent reduction in radiation to the ovaries and fetus.

[It is felt the distributors of the LogEtron, as well as various experienced operators, would object to the implication of "enhancement of detail," as there is great loss of detail on the roentgenogram in bringing the density of the film to the optimum viewing level.—R. L. E.]

Seven roentgenograms; 2 diagrams; 1 table.
ROBERT L. EGAN, M.D.
University of Texas, Houston.

THE GENITOURINARY SYSTEM

Wilms' Tumor in a Horseshoe Kidney. A Case Report. John B. Lawlor, John K. Lattimer, and James A. Wolff. Pediatrics **23:** 354–358, February 1959. (J. B. L., 454 Angell St., Providence, R. I.)

A case of Wilms' tumor in a horseshoe kidney is added to the 6 previously recorded in the English literature. This case illustrates the difficulty in the clinical and roentgenographic differentiation between tumor in a horseshoe kidney and hydronephrosis with nonfunction of an occluded supernumerary renal pelvis. Retrograde pyelography was necessary to clarify the diagnosis.

The patient, a 3 1/2-year-old girl, survived fourteen months after surgery. She had six courses of irradiation, including supervoltage therapy (betatron); the total dosage is not given. Necropsy revealed perforation of the distal ileum with fecal peritonitis and metastases to the liver, stomach, peritoneum, and uterus. The terminal events in this child, namely, fecal fistula and peritonitis, illustrate the possible effects of radiotherapy in Wilms' tumor. Although metastases were found at necropsy, reconstruction of the history and later course suggests sudden rupture of the heavily irradiated small bowel, leading to peritonitis with overwhelming sepsis. It is recognized, of course, that large doses of radiation offered the only possible hope of cure in this patient.

Two roentgenograms.

Ureterocele and Prolapse of the Ureter. L. Wemeau, G. Lemaitre, and G. Defrance. J. de radiol. **40:** 275–276, May 1959. (In French)

Ureterocele consists of a cystic dilatation of the inferior extremity of the ureter so that it bulges into the bladder, the bulge being covered by bladder mucosa. Near the inferior pole of the ureterocele lies the ureteral orifice. The condition occurs relatively frequently in children and may be associated with other anomalies such as duplications.

If the ureteral meatus is normal, the upper urinary tract is relatively normal and the ureterocele is recognized as a small "cobra head" filling defect in the

cystogram. If the meatus is stenosed, the ureterocele enlarges considerably, with dilatation and perhaps infection of the upper tract. It may encroach upon the opposite ureteral orifice.

In the very rare prolapse of the ureter, the filling defect in the bladder is rectangular or cylindrical, extending obliquely downward toward the vesical neck, and the projecting bulge is covered by ureteral mucosa. In a 30-year-old female there was obstruction of such degree that only a nephrogram was obtained on the ipsilateral side on intravenous urography.

Retrograde cystography with incomplete distention of the bladder is recommended to demonstrate these conditions.

Two roentgenograms; 1 diagram.

CHARLES M. NICE, JR., M.D., PH.D.
Tulane University

Congenital Posterior Urethral Valves: A Study of Thirty-Five Cases. W. I. Forsythe and G. D. F. McFadden. Brit. J. Urol. **31:** 63–70, March 1959. (Royal Belfast Hospital for Sick Children, Belfast, Ireland)

Congenital valvular obstruction of the posterior urethra in males is seen mainly in infants and young children, but the condition may go unrecognized until adult life, when irreversible changes have occurred in the kidneys as a result of back pressure and/or infection. The authors report 35 cases seen in the past five years. Six of the patients were under three years of age; the remainder were between three and sixteen.

Anatomically, posterior urethral valves are of three main types, depending on their relation to the verumontanum (Young, *et al.* J. Urol. **3:** 298, 1919): Type I, passing from the distal end of the verumontanum to the lateral urethral wall; Type II, forming partial or complete diaphragms arising (*a*) proximal to the verumontanum, (*b*) distal to the verumontanum, or (*c*) at the verumontanum and passing laterally to the walls of the urethra; Type III, arising from the proximal end of the verumontanum and passing upward to the bladder outlet. In this last type the valves usually consist of low ridges and are nonobstructive. In the present series, the valves were of Type I in 32 patients, Type II *b* valve in 1, and Type II *c* in 2.

The clinical picture associated with posterior urethral valves varies with the degree of urethral obstruction, the effect of back pressure on the kidneys, the presence or absence of infection, and the age of the patient. In the children under three years of age, acute retention, difficult or hesitant micturition, vomiting, and dribbling were the main symptoms, and a palpable bladder, abdominal distention, and pyuria, the main signs. In children over three, frequency was the most common complaint; difficult or hesitant micturition and nocturnal and diurnal enuresis were common. Seven of this older group had hematuria; in 3 it was the presenting symptom and in 1 it was associated with urinary infection. Six patients had palpable bladders and 10 had pyuria. In 6 of the authors' cases, nocturnal enuresis disappeared but was replaced by nocturnal frequency.

With the technic of micturition cystography described by Fisher and Forsythe (Arch. Dis. Childhood **29:** 460, 1954), not only may the valves be demonstrated as a constant constriction or filling defect but they may be accurately localized, and this is of great assistance to the surgeon at operation. In 20 patients in the present series the bladder capacity was found to be normal; in 2 it was increased to 350 and 450 ml., respectively; and in 6 it was below normal. Figures for the others are not available. The posterior urethra was elongated and dilated in 11 patients; in 9 of these there was widening of the internal sphincter. One patient had narrowing of the internal sphincter but no urethral elongation. There was trabeculation of the bladder in all but 8 cases; 2 of these showed widened internal sphincters, 2 marked elongation and dilatation of the posterior urethra proximal to the valves, and 1 several small diverticula. In addition, diverticula were demonstrated in 3 cases and multiple diverticula in 1. A right vesico-ureteral reflux was present in 3 patients and a left vesico-ureteral reflux in 4. There were 5 patients with bilateral hydro-ureter and hydronephrosis.

Of the 35 patients in this series, 30 have been under observation for more than a year and 25 for more than two and a half years since operation. Of the 6 children under three, 1 died before surgery, 2 are cured, and 3 have occasional urinary symptoms. Of the 29 over three, 14 are cured, 2 improved, and 8 unchanged. Five children operated on during the six months prior to the report are not included in the results.

Five cystograms; 1 drawing; 1 table.

Radiologic Aspects of Calcifications of the Male Genital Tract. Jacques Wangermez. J. de radiol. **40:** 236–242, May 1959. (In French) (Bordeaux, France)

The ductus deferens ascends upward and laterally from the scrotum, then turns medially and descends into the ampulla deferens just above the seminal vesicle. The latter two empty into the ejaculatory duct which descends to enter the prostatic urethra. Calcification occurs in the wall of the ductus and ampulla and is usually due to diabetes. Bilateral calcification of the ampulla is commonly associated with impotence. The calcified ampulla forms a curve like the "horn of a yak."

Calcification in the seminal vesicles occurs in the form of concretions which produce an elongated oval density within the lumen. The condition is usually associated with chronic infection, especially tuberculosis. Calcification commonly occurs in one wall of the ductus deferens, which will aid in differentiating it from the parallel dense lines of arterial calcifications. If both walls are calcified in the scrotal portion, the ductus will be wider than the accompanying artery.

Prostatic calcifications are of two types: multiple small symmetrically disposed calculi in normal glands and the usually solitary calculus in a newly-formed prostatic diverticulum. The diverticular prostatic calculus must be differentiated from calcification in the seminal vesicle, which is usually larger and more elongated and is situated above and posterior to the prostate. The latter aspect may be accentuated by the Trendelenburg position. Diverticular prostatic calculi are usually of infectious origin. The etiology of glandular calculi remains obscure.

Nine roentgenograms; 1 diagram.

CHARLES M. NICE, JR., M.D., PH.D.
Tulane University

A New Catheter for Urethrography. Allan Tauber. J. Urol. **81:** 700–701, May 1959. (8820 Wilshire Blvd., Beverly Hills, Calif.)

The author describes a simple new catheter for

performing urethrography. This consists of a terminal eye catheter with a constricting coronal band attached to it by guy bands. The tip of the catheter fits into the urethral meatus and is held in place by the band, which is wrapped around the penis and held by a hemostat.

Advantages of the catheter are ease of use and ready cleansing and sterilization. It is comfortable for the patient and keeps the examiner's hands at some distance from the x-ray beam.

One roentgenogram; 3 photographs.

RICHARD H. GREENSPAN, M.D.
University of Minnesota

Intravenous Hydrocortisone in the Treatment of a Severe Urographic Reaction. F. W. Wright. Brit. J. Radiol. **32:** 343–344, May 1959. (Radcliffe Infirmary, Oxford, England)

The author reports a case of a 31-year-old man, in whom a severe vascular reaction occurred seven minutes after the intravenous injection of Hypaque. The patient was essentially healthy and gave no history of asthma, hay fever, nor any other sensitivity. He was not given a test dose of the medium. The reaction consisted in chest pain followed by shock and unconsciousness. Antihistamine, 10 mg., injected intravenously had no appreciable effect, but an intravenous injection of 100 mg. of hydrocortisone produced immediate improvement; the patient was conscious within one minute and able to return home after three hours.

The author refers to a case of pulmonary edema following angiocardiography responding to hydrocortisone (Besterman, Leonard, and Wood. Brit. M. J. **2:** 695, 1956) and also quotes Weigen and Thomas on the use of the drug (Radiology **71:** 21, 1958). It may be life-saving in the event of a severe reaction and should be on hand in all departments of radiology.

J. S. ARAJ, M.D.
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THE LYMPHATICS

Normal Roentgen Anatomy of the Lymph Vessels of Upper and Lower Extremities. Sten Jacobsson and Sven Johansson. Acta radiol. **51:** 321–328, May 1959. (Malmö Allmänna Sjukhus, Malmö, Sweden)

The normal roentgen anatomy of the lymph vessels of the arms and legs was investigated in 80 volunteer subjects without known diseases of the limbs, by a clinical method described by Kinmonth (see Kinmonth, Taylor, and Harper. Brit. M. J. **1:** 940, 1955. Abst. in Radiology **66:** 311, 1956).

Two groups of lymphatics, radial and ulnar, were observed in the upper limb. Axillary lymph nodes were well demonstrated by injection of contrast material in the region of the elbow, but were poorly seen when the injection was made in the carpal area. Lymph nodes in the region of the elbow were not filled in any instance.

In the leg, two lymph vessel groups were demonstrated, the saphena magna and saphena parva systems. The former system in the lower leg consists of a medial and a lateral group, and filling of either or both groups was often obtained by injecting a vessel on the dorsal aspect of the foot. The lateral group contains more vessels, and these divide more frequently, than the medial group. Both groups course toward the medial aspect of the knee, and then accompany the saphena magna, dividing frequently before emptying into caudal inguinal lymph nodes. The vena saphena parva system consists of one to three lymph trunks coursing along the back of the lower leg and emptying into popliteral lymph nodes. Efferent vessels from the latter nodes course anteriorly and medially and accompany the saphena magna group to the groin to empty into lymph nodes situated deeper than those draining the saphena magna group, and more cranial. There was no evidence of communication between the two systems.

Inguinal lymph nodes were best demonstrated by exposures made immediately after a rapid injection of a large amount of contrast material.

Despite branching, the width of the vessels does not change appreciably. The diameter of the trunks visualized varied from 0.25 to 1.0 mm. Valves appeared as distinct rounded swellings from 0.5 to 1.0 cm. apart. The lymph vessels did not show abrupt interruption, marked tortuosity, retrograde filling, or centripetal arborization. Accumulations of contrast material outside normal lymph vessels may occur as a normal variant. No explanation is offered for this phenomenon.

Thirteen roentgenograms.

SAMUEL B. HAVESON, M.D.
Lynwood, Calif.

Practical Value of Lymphography of the Extremities. G. Arnulf. Angiology **9:** 1–6, February 1958. (41 Rue St. Heléne, Lyon, France)

The author discusses the technic and value of lymphography of the extremities in the dog and in man.

Direct injection of contrast medium into the lymphatics is not possible in all cases because the vessels are sometimes too small. Thorotrast, injected subcutaneously, has proved a satisfactory contrast medium for lymphography in dogs. In man, however, the Thorotrast remains *in situ*, and it has been found necessary to employ the Kinmonth technic (see, *e.g.*, Brit. M. J. **1:** 940, 1955. Abst. in Radiology **66:** 311, 1956). With this method, prior to the introduction of a radiopaque medium, the lymphatics are made visible to the naked eye by the subcutaneous injection of a diffusible dye. A contrast agent is desirable which, when injected subcutaneously, will diffuse into the human lymphatics in the manner that Thorotrast is diffused in the lymphatics of the dog.

The normal lymphatics are extremely tenuous. They appear as a fine network rising along the extremity. When injection is made into the lymphatics of the back of the foot, some small threads are seen extending upward at the inner edge of the leg and of the thigh. The passages are more or less sinuous, with small bulges all along their course, reminding one of the classical anatomical picture. The ganglia are equally visible.

At present, the only clinical value of lymphography seems to be in the study of lymphedema. Two groups of patients are seen, those with normal lymphatic and those with enormous dilatations (dilated and sinuous lymphatics). Lymphangiography permits the identification of those cases which actually result from an obstruction of the lymphatic pathways.

Eleven roentgenograms; 5 photographs.

MISCELLANEOUS

Cervical Medullary Atrophy. Rôle of Gaseous Myelography. G. Bonte, C. Delfosse, P. Warrot, and H. J. Martin. J. de radiol. **40:** 268–270, May 1959. (In French) (Hôpital régional, Lille, France)

A 38-year-old man was seen with muscular weakness and sensory dissociation of the upper extremities, sensory changes in the left lower extremity, and early spasmodic paraplegia. Routine roentgenograms and a myelogram with Lipiodol were normal. A repeat myelogram with 12 c.c. of Discolipiodol showed, instead of the usual filling defect produced by the cervical cord, a slender sinuous filling defect, suggesting a thinning of the cord. Gaseous myelography performed according to Murtagh *et al.* (Am. J. Roentgenol. **74:** 1, 1955. Abst. in Radiology **66:** 793, 1956) revealed more distinctly the narrowing of the cervical cord, apparently due to a primary degenerative process of unknown etiology.

CHARLES M. NICE, JR., M.D., PH.D.
Tulane University

Radiographic Characteristics of Glass. Warren C. Roberts. Archives of Industrial Health **18:** 470–472, December 1958. (137–47th St., Niagara Falls, N. Y.)

Some roentgenologists are of the opinion that glass, when buried in the human tissues as a foreign body, will not be visible on x-ray film unless it contains some lead. This problem has been investigated. It was found that the radiographic density of common glasses does not depend on their lead content, but on their density or specific gravity. Glass is denser than tissue, and even a fragment of 0.1 mm. can be seen in the tissues of the hand. If par-speed screens are used, they must be clear of all defects and dust. Otherwise cardboard holders should be employed. Dental film placed against the nose can be used for foreign bodies in the anterior chamber of the eye.

If laboratory glassware, which rarely contains lead, is driven into a flesh, a negative x-ray report should be accepted as fairly conclusive that the glass is not still in the tissue.

Four roentgenograms.

RADIOTHERAPY

Supervoltage (2 Mev.) Rotation Irradiation of Carcinoma of the Head and Neck. Milton Friedman, Martha E. Southard, and William Ellett. Am. J. Roentgenol. **81:** 402–419, March 1959. (1016 5th Ave., New York 28, N. Y.)

One hundred and forty-three patients with 147 carcinomas of the head and neck were treated with 2-Mev roentgen rays between 1951 and 1957. With the exception of a few salivary gland and nasal tumors, the lesions were squamous-cell carcinomas. Sixty-seven per cent of the patients received rotation therapy and 33 per cent were treated through stationary portals.

For each patient a model of body contour at the level of the lesion was constructed. An isodose distribution pattern was then made with the aid of film densitometry and checked with random ionization chamber measurements. A study of 150 isodose distribution patterns showed four predominant types: (1) a small cylinder of high dosage irradiation completely immersed in tissue; (2) a small, partially immersed cylinder; (3) "in-continuity" irradiation, the cylinder being completely immersed at the level of the primary tumor and partially immersed at the lymph-node level; (4) a large partial cylinder for "in-continuity" irradiation.

The first type is used in the nasopharynx, nasal sinuses, and oropharynx, where the primary lesion is central and treated separately from the nodes. The fall-off of dosage peripheral to the cylinder is rapid. If the cross section of the cylinder is large, the fall-off is slower, the tissue dose to certain points in the adjacent normal tissue is higher, and the "index of efficiency" is lowered. In antral lesions sector radiation had no advantage over complete rotation in sparing the opposite eye. The authors have seen no cataracts even with doses of 4,000 to 5,000 rads to the opposite eye. This risk, however, is yet to be evaluated by time. In the vertical axis, protection of the eye is best achieved by collimation of the beam.

The second pattern—the partially immersed small cylinder—is used for lesions near the surface that require large lethal doses, *e.g.*, parotid gland cancer and cervical metastases. The index of efficiency is high, and large tumor doses can be given. There is a small advantage in using a 180° sector rather than 360°.

"In-continuity" irradiation with the cylinder completely immersed at the level of the primary tumor and partially immersed at the level of the cervical metastases is used for carcinoma of the tonsil, posterior margin of the tongue, and the lateral wall of the oropharynx, when the area involved does not occupy a large cross section of the head and neck. With a small cylinder there is a high index of efficiency and large doses can be given.

"In-continuity" irradiation with a large partial cylinder is the most popular technic and is used for the tonsil, tonsillar pillars, tongue, and oropharynx when the primary lesion is large or reaches the midline and there are multiple regional metastases; when an entire node area with or without the primary lesion is to be treated; and when the areas of primary disease and lymph node metastases are widely separated. With a partial cylinder the radiation can be kept unilateral, and a large dose can therefore be tolerated. In applying a unilateral technic, however, a well collimated beam is important. Few of the commercially available Co^{60} teletherapy units are capable of producing a sharply delineated cylinder of high dosage irradiation. Most high-energy roentgen ray machines, on the other hand, have efficient collimators.

Stationary ports were used predominantly in (1) midline neck lesions where all the disease plus a minimal amount of normal tissue could be irradiated; (2) bilateral regional node metastases that could be included in the ports for the primary lesion; (3) some cases with unilateral regional metastases that could be covered by the primary port.

Dosage was guided by records of epithelial reaction

and tumor shrinkage curves obtained with 6,000 r at 250 kv. To obtain the same results in the same period as much as 33 per cent more irradiation with supervoltage and as much as 50 per cent more with rotational technic was necessary. The most common figures in this series were 6,500 to 10,000 rads in thirty to thirty-five days.

In contrast to popular opinion the incidence of bone and cartilage necrosis was similar to that obtaining with orthovoltage.

Supervoltage rotation therapy is especially useful for multiple primary lesions, as a high dose can be placed next to a previously treated lesion.

The number of cases of each type of lesion was too small for statistically significant conclusions, but some useful impressions were gained: (1) Carcinoma of the tonsil was consistently sensitive. (2) In 16 carcinomas of the anterior two-thirds and margin of the tongue treated with supervoltage irradiation the results were unsatisfactory. The median tumor dose was 8,400 rads in thirty-nine days, which is probably the minimal lethal dose. This lesion is now treated interstitially. (3) Four of 5 parotid cancers did not show shrinkage despite enormous doses (9,625 to 10,253 rads). Orthovoltage has been more satisfactory and, until further evidence to the contrary is obtained, is to be preferred. (4) A completely immersed small cylinder for recurrence of laryngeal cancer around the tracheostomy stoma gave promising results in 2 cases. (5) Most lesions were extensive. Three-year arrest rates were slightly higher for recurrent than for primary tumors. This suggests special merit of supervoltage rotational therapy for recurrent lesions of the head and neck. (6) In this series, containing mostly advanced lesions, overall results were relatively favorable. The three-year absolute arrest rate was 33 per cent, and the five-year rate was 29 per cent.

Sixteen figures; 9 tables.

VAHE MEGHROUNI, M.D.
Los Angeles, Calif.

Therapy of Malignant Struma. P. Veraguth. Radiol. clin. **27:** 293–308, September 1958. (In German) (Röntgeninstitut der Universität Bern, Switzerland)

Despite its title, this paper treats only of the various procedures required prior to the administration of any kind of therapy in suspected thyroid cancer. The author insists on (1) careful inspection and palpation of the region of the neck, (2) detailed search for distant metastases—routine chest roentgenogram in every case and sometimes bone surveys; (3) radioiodine procedures, including a scintigram of the neck, scanning of the entire body for iodine-concentrating metastases, and a thyroid-uptake determination; (4) thyroid biopsy, after the administration of radio iodine so that tissue uptake can be assessed.

Three roentgenograms: 2 photographs; 9 scintigrams; 2 diagrams; 1 table.

E. R. N. GRIGG, M.D.
Cook County Hospital, Chicago

Combined Radiologic-Surgical Treatment of Carcinoma of the Cervix. Thor Dahle. Surg., Gynec. & Obst. **108:** 600–604, May 1959. (Norwegian Radium Hospital, Oslo, Norway)

In the years 1954–1956, 226 patients were admitted to the Norwegian Radium Hospital with Stage I carcinoma of the cervix. Of these, 96 received radium treatment followed by radical surgery.

All patients were primarily given radium therapy—6,000 to 7,200 mg. hr. (30 mg. in the vagina and 25 to 30 mg. in the uterus for five days). Those selected for radical surgery were then discharged from the hospital and re-admitted six to eight weeks later. At that time a radical hysterectomy, with bilateral pelvic lymph node dissection, was done. The patients not selected for combined therapy were given a complete course of x-ray therapy, each receiving 3,000 r skin dose to each of two posterior and two anterior portals.

The surgical specimens in all cases were studied pathologically. Sixteen showed residual carcinoma of the cervix and 18 showed lymph-node metastasis. In 12 of the latter group there was no residual carcinoma in the cervix. In view of these observations, the author points out the unreliability of clinical staging, since 18.75 per cent of supposedly Stage I carcinomas had lymph node metastases. He also notes that cervical biopsy would be an unreliable indication of the extent of the disease in the 12 cases with node metastases.

The author does not attempt to evaluate his total results at this early date. He does, however, report that there were no operative deaths and that, of the 96 patients, 12 were dead as of June 1, 1958. Nine of these 12 had originally shown lymph-node metastases. Two of the other 3 died of recurrent disease and 1 of bilateral pyonephrosis with no evidence of pelvic metastasis at autopsy.

An attempt was made to study all of the patients by urography for damage to the ureters. Sixty-two of the 96 patients showed no urographic abnormalities. Abnormalities were found in 22, as follows: 4 ureteral fistulas, 1 nonfunctioning kidney, 1 bilateral pyonephrosis (subsequently fatal), 5 cases of hydronephrosis, and 11 cases of slight hydroureter or slight hydronephrosis. The author believes that most of these urographic abnormalities were caused by the combined surgical-radiologic therapy and this fact should be borne in mind when one is reflecting on the value of such treatment.

Seven figures, including 3 roentgenograms; 3 tables.

WALLACE T. MILLER, M.D.
University of Pennsylvania

Management of Recurrent Carcinoma of the Cervix. E. J. Love and H. H. Allen. Am. J. Obst. & Gynec. **77:** 539–545, March 1959. (University of Western Ontario, London, Ont., Canada)

One hundred and eighteen cases of residual or recurrent carcinoma of the cervix are reported. The primary method of treatment was radiotherapy, consisting of intrauterine and vaginal radium therapy followed by cobalt-60 irradiation to the parametria (formerly conventional x-ray therapy was used). This treatment gives a dosage of approximately 8,500 rads to Point A and 5,500 rads to Point B. Of 210 patients with primary carcinoma of the cervix treated from 1949 to 1954, 110 (52.4 per cent) are alive and well.

Radiation failures are divided into two classes: (1) residual carcinoma—cases in which evidence of disease appears within the first six months following the primary treatment—and (2) recurrent carcinoma—lesions in which recurrence is diagnosed more than six months after the beginning of treatment. Ninety-six

of the recurrent cases were treated by re-irradiation between 1949 and 1954; 4 of the patients (4 per cent) survived longer than two years.

Between 1955 and 1957, 22 cases of recurrence were selected for surgery. In almost every instance, the stage of the recurrence was higher than of the original disease. It is believed that this situation could have been improved by closer follow-up and by more prompt action when recurrence was suspected. Four patients were found to be inoperable. Hysterectomy supplemented by node dissection was carried out in 9 patients, and 6 are alive and well. Exenteration and node dissection were performed in 9 patients, of whom 3 are alive and well.

The authors believe that an increase in the survival rate of patients with recurrent carcinoma of the cervix can come only with earlier laparotomy in cases where suspicious signs or symptoms are present.

Nine tables.

The Terminal Findings in Endometrial Carcinoma. M. L. Bunker. Am. J. Obst. & Gynec. **77:** 530–537, March 1959. (University of Toronto, Toronto, Ont., Canada)

A detailed survey of 44 cases of endometrial carcinoma that came to autopsy is presented The survey covered a period of thirty years. Nearly one-half of the patients had been admitted to the hospital with a diagnosis other than endometrial carcinoma, the latter condition being discovered during the hospital stay or uncovered at the time of death. In one-half of the cases medical complications precluded any definite therapy; only 11 patients had definitive treatment, in the form of hysterectomy or surgery plus radium or other radiation. The remaining patients received no treatment or only palliative measures. In 34 patients extrapelvic extension of the disease was noted at the time of death.

The primary causes of death were: carcinomatosis in 12 cases, peritonitis in 15, intestinal obstruction in 3, bronchopneumonia in 3, cardiac disease in 4, uremia in 2, and miscellaneous conditions in 5 cases. Metastases were widespread, involving the brain, lung, liver, stomach, spleen, adrenal, kidney, gallbladder, small and large bowel, rectum, ureter, bladder, tubes, and ovaries. There were no demonstrable skeletal metastases.

Adjacent organs, as the bladder, rectum, tube, and ovary, showed a high incidence of involvement. Spread to the lower urinary tract and rectum occurred across cleavage planes, usually with carcinomatosis due to hematogenous spread. The thin-walled blood vessels of the uterus were easily invaded by cancer cells, and such invasion always resulted in the death of the patient.

Spread of the carcinoma to nodes and organs above the brim of the pelvis was as common as, if not more common than, spread to the adjacent nodes and organs. For this reason, the value of extension of surgical treatment of endometrial carcinoma to include the pelvic nodes appears questionable. When the cervix was involved, the spread of the disease was along the same channels as that of cervical carcinoma.

Rapid progression of the cancer resulting in the death of the patient usually manifested itself within the first year after treatment.

Two figures; 9 tables. ROBERT L. EGAN, M.D.
University of Texas, Houston

Cancer of the Vulva. Analysis of Results of Treatment During the Years 1935–1955. Bent Langfeldt-Andersen. Acta radiol. **51:** 369–378, May 1959. (Radium Centre for Jutland, Aarhus, Denmark)

One hundred and sixty-five cases of cancer of the vulva seen in the Radium Centre for Jutland from 1935 to 1955 are analyzed; 139 of these (84.2 per cent) were postmenopausal. Carcinoma accounted for 92 per cent of the series, sarcoma for 7.4 per cent. In 2 cases there was no histologic examination; in 1 other, precancerous changes were found. Of the 12 sarcomas, 9 were malignant melanomas. Leukoplakia was observed in 21.2 per cent of the cases, syphilis in only 1.2 per cent; no instances of lymphogranuloma inguinale or condyloma acuminatum were seen. More than a third of the patients (38.8 per cent) sought medical attention a year or more following appearance of the tumor.

Of the 165 cases, 2 were excluded from the analysis of results because of postoperative death and 4 others were not treated; 138 of the remaining 159 patients were followed for five years or more.

Three methods of treatment were employed: (1) electrocoagulation, in some cases supplemented by radiotherapy; (2) partial or complete vulvectomy with dissection of inguinal lymph nodes and, in most cases, postoperative radiotherapy; (3) radiotherapy, supplemented by electrocoagulation in some cases. The overall five-year survival without recurrence was 23.2 per cent. Five-year survival without recurrence in the group treated by electrocoagulation was 24.2 per cent, in those treated by vulvectomy 31.3 per cent, and in those treated primarily by radiotherapy, 4.1 per cent. The last group consisted almost exclusively of old patients with extensive tumors.

It is pointed out that this series covers a period of twenty years, and that treatment principles have changed considerably during that interval. Furthermore, the series contained a large number of advanced cases. Fifty-nine of the patients were treated during the years 1948 to 1955. Three-year tumor-free survival in this group was 34.4 per cent following electrocoagulation, 43.8 per cent following vulvectomy, and 18.2 per cent following radiotherapy. The author concludes that (1) complete vulvectomy with node dissection is the method of choice in cancer of the vulva; (2) electrocoagulation is useful in very small tumors or more extensive superficial tumors; (3) radiotherapy is indicated only as a palliative procedure.

Eight tables. SAMUEL B. HAVESON, M.D.
Lynwood, Calif.

Wilms Tumor: A Report of 45 Cases and an Analysis of 1,351 Cases Reported in the World Literature from 1940 to 1958. Hans J. Klapproth. J. Urol. **81:** 633–648, May 1959. (Cleveland Clinic Foundation, Cleveland, Ohio)

The author reviews 45 cases of Wilms' tumor from the Cleveland Clinic and a large number of cases from the world literature. The pathology of the tumor is discussed in some detail. Invasion of the renal vein has been observed frequently, occurring in no less than 45 per cent of one reported series. Other sites of metastasis are the liver, bones, and contralateral kidney. Local recurrences or metastases usually occur early, in the majority of the cases within one year after surgical intervention.

The greater part of this article discusses the experi-

ence of the author and of those contributing to the world literature in regard to treatment of Wilms' tumor. The results of nephrectomy alone fall far short of those achieved by the combination of surgery and radiotherapy. It does not appear to make a significant difference as to whether radiotherapy is utilized before or following surgery or whether it is used both pre- and postoperatively. The cure rate utilizing the combination of radiotherapy and surgery is approximately 25 per cent.

Two hundred eight references are appended.

One graph; 10 tables.

RICHARD H. GREENSPAN, M.D.
University of Minnesota

Discussion on Testicular Tumours. Arthur Jacobs, A. C. Thackray, and Thomas M. Prossor. Proc. Roy. Soc. Med. **52:** 336–343, May 1959. (A. J., Glasgow, Scotland)

Jacobs, introducing this discussion of testicular tumors, outlines the overall clinical approach and indicates pertinent questions at issue on treatment. Important points made include the following: Less than 1 per cent of all malignant tumors occur in the testis. Various series indicate that about 15 per cent of the total number are in undescended or maldescended testes. Previous tuberculous disease (tuberculous epididymitis) may obscure the diagnosis. Local extension to adjacent tissues is of little real importance in this disease, since the lesion shows a strong tendency to remain well confined. The important route of dissemination is through lymphatic channels. Renal pedicle nodes are frequently the primary site of metastases because of the efferent lymphatic channels accompanying the spermatic vessels. Nodes in the region of the iliac vessels may become involved when the tumor invades the epididymis, as the lymphatic channels from this structure drain to the iliac nodes. The prognosis must be based on the most malignant component of the tumor shown on histologic study. The more primitive the tumor the greater its frequency and extensiveness of spread.

In Britain the accepted treatment for testicular tumors is simple orchiectomy including a segment of the spermatic cord, followed by deep x-ray therapy. In a relatively small series reviewed by the author the four-year survival rate for seminoma was about 85 per cent with this combined treatment. With other tumor groups, which tend to be highly malignant and radioresistant, five-year arrests lie between 20 and 50 per cent. The author notes that in America the radical operation (retroperitoneal lymph-node resection) is more popular and that generally deep x-ray therapy is given only if the excised nodes are found to be positive.

Thackray discusses nomenclature and classification. He laments the fact that there is no agreed upon international classification for testicular tumors and notes the consequent difficulty in comparison of therapeutic results. The main pathologic types, which he lists as teratoma, embryonal carcinoma, and seminoma, are briefly described. Choriocarcinoma is included with the embryonal group.

Prossor discusses the role of radiotherapy in malignant disease of the testes. He notes that medical opinion in Britain is almost solidly against attempts at radical operation; simple orchiectomy and deep x-ray therapy, as stated by Jacobs, are considered the treatment of choice. Some American authorities have recommended the radical operation in the treatment of radioresistant tumors.

Prossor's remarks are based on a series of 318 cases reviewed by him. He points out that anatomical studies by others indicate that the arrangement and nature of the lymphatics of the testes are such as to render their complete surgical removal exceedingly difficult, if not impossible. He uses these facts to explain the high failure rate of the radical operation and to indicate also the fields that should be used in the treatment by postoperative irradiation. He proceeds on the assumption that all of the drainage nodes from the testis are potentially involved and treats them in all cases. Radiotherapy is not directed to the chest unless the findings indicate metastases there. Radiosensitivity of some tumors may prove so great that the disease can be controlled for long periods by radiotherapy, even in the face of extensive metastases involving the chest and supraclavicular areas. The relative advantages of supervoltage therapy over conventional voltages are cited.

Radiotherapeutic technics are briefly summarized. The author favors treatment through extensive large fields essentially irradiating the entire torso from the level of D-12 to the groin. He describes an arrangement with two large anterior rectangular fields 30 × 20 cm., angled at 120° to each other, and a circular posterior field 30 cm. in diameter. It is admitted that such a large volume dose may produce adverse side effects. The aim is a minimum tumor dose of 3,000 r in four to five weeks, but frequently the patient cannot tolerate this, even with the relatively radiosensitive seminomas. Consequently, the tendency is toward the use of smaller fields with higher-voltage therapy; this becomes essential if the tumor is other than seminoma. The hazard of radiation nephritis is commented upon: wide-field therapy with a tumor dose of over 2,000 r in five weeks or less is definitely risky.

In a few comments as to results, the author notes 75 per cent five-year survivals in patients with seminoma with no initial clinical evidence of metastases. The figure drops to 46 per cent for similar groups with teratoma managed by simple orchiectomy and postoperative radiotherapy. For this more resistant tumor, depth doses of 4,500 to 5,000 r in thirty days are favored, through longer and narrower rectangular fields, with 2-Mev x-rays. Tumor doses in the 4,500 to 5,500 r range in six weeks with supervoltage therapy appear well tolerated in the abdomen and pelvis allowing "very satisfactory and even lasting regression of abdominal metastases from teratoma."

Therapeutic results are summarized in 5 short tables. It is evident that both stage of the disease and histologic type are of critical importance in formulating prognosis.

Three photomicrographs; 5 tables.

JAMES W. BARBER, M.D.
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Treatment of Malignant Testicular Tumors at the Norwegian Radium Hospital. Herman Host and Torvald Stokke. Cancer **12:** 323–329, March-April 1959. (Norwegian Radium Hospital, Oslo, Norway)

The authors review the results of treatment in 300 patients with malignant testicular tumors seen at the Norwegian Radium Hospital between 1932 and 1953. The average age for the group was thirty-seven years, with a range from six months to seventy-three years.

The five-year survival for the series was 58 per cent. Division of the period into three phases revealed improvement in results, from an early five-year survival rate of 50 per cent to 72 per cent for 1949–1953. Much of this improvement was due to increased survival of patients with seminoma (from 68 per cent in 1932–1942 to 84 per cent in the last phase).

On the basis of their own experience, and that of others, the authors consider the most rational treatment for seminoma to be orchiectomy followed by prophylactic irradiation. Their data indicate somewhat larger dosage than is usually recommended. Patients now receive a skin dose of 3,500 to 4,000 r, to deliver a tumor dose of 2,700 r or more to the lumbar nodes.

The embryonal carcinomas and teratomas are more highly malignant and radioresistant than the seminomas. Orchiectomy combined with radical glandular toilet, including removal of retroperitoneal nodes, was used for 16 patients, most of these receiving supplementary postoperative x-ray treatment. This radical treatment did not seem to improve prognosis.

Metastases were demonstrated at the time of primary treatment in 65 patients, 12 of whom survived five years (19 per cent). Nine of the 12 had seminomas. The five-year survival for the entire group of seminomas with metastases was 38 per cent (9 of 25).

The frequency of bilateral testicular tumor has been placed at about 2 per cent. Of the 300 patients in this series, there were 10 in whom a malignant tumor developed in the contralateral testicle a shorter or longer time after the primary treatment, indicating that once a patient has a testicular tumor, the probability of a secondary development contralaterally is greater than for unilateral development of the disease in normal persons.

One graph; 6 tables.

CHARLES M. GREENWALD, M.D.
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Radiation Treatment of Chronic Leukemias. N. G. Godekar. Indian J. Radiol. **13:** 77–103, May 1959. (All-India Institute of Medical Sciences, New Delhi 16, India)

The author discusses in a general way the clinical manifestations, etiology, classification, and diagnosis of leukemia. His own series numbers 77 cases, of which 82 per cent were chronic myeloid leukemia, while only 18 per cent were chronic lymphatic leukemia. In the western world the ratio of the two types is about equal. This difference is explained by the lower population age in India, since myeloid leukemia is commoner in younger people than lymphatic.

All 77 patients were treated by external irradiation to the spleen, liver, or bone marrow. Some had splenic irradiation alone and in others all three areas were irradiated. A table summarizes the symptoms, laboratory tests, treatment, and follow-up in every case of the series. None of the patients were given chemotherapy.

The author's findings agree with the accepted view that irradiation can produce remissions and improve the general well-being of patients suffering from leukemia, but his follow-up was inadequate for conclusions concerning the effect upon survival.

Four roentgenograms; 5 graphs; 6 tables.

J. S. ARAJ, M.D.
Toledo, Ohio

Electron Therapy at 8 MeV. A. Batchelor, D. K. Bewley, Robert Morrison, and J. A. Stevenson. Brit. J. Radiol. **32:** 332–338, May 1959. (Hammersmith Hospital, London, W. 12, England)

When the 8-Mev linear accelerator is used for x-ray therapy, an electromagnet deflects the electrons through a right angle before they strike the target. If the magnet is not energized, the electrons continue in a straight line, emerging as a 1-cm. pencil of radiation. This passes through a scattering foil of gold, 0.11 mm. in thickness. The resultant divergent beam is confined by a Dural cylinder. A stop near the machine end limits irradiation of the cylinder wall to the last third, and a 1.6-mm. aluminum diaphragm at the other end defines the treatment field. Perspex walls a few centimeters in length intercept scattered electrons between the diaphragm and the patient's skin, thus improving the sharpness of the edge of the field. It is also possible to define the beam with a lead mask 3.7 mm. in thickness, but this gives an x-ray dose amounting to 2.5 per cent of the electron dose, as compared to 1 per cent for aluminum. If a less penetrating beam is wanted, a block of carbon is substituted for the scattering foil. Because of the enormous dose rates that the machine can provide, special precautions are taken to prevent accidental overdosage of a patient.

The integrated dose to the patient is monitored by a pair of ionization chambers at the end of the Dural tube. The standard for dosimetry is a Baldwin-Farmer substandard dosemeter with the chamber at a depth of 1.5 cm. in a tissue-equivalent phantom. This is calibrated against radium, and (at the National Physical Laboratory) with a 2-Mev generator.

Isodose curves measured in a water phantom are given. In the first 2.4 cm. below the surface the dose is relatively uniform, and this is considered the zone of therapeutic usefulness. The rapid fall-off beyond this depth results in integral doses which are small compared to x-ray or radium therapy.

A few examples of treated cases are given.

Twelve figures; 1 table.

LUCILLE DU SAULT
The Henry Ford Hospital

A Technical Advance in Irradiation Technique. Anthony Green. Proc. Roy. Soc. Med. **52:** 344–346, May 1959. (London, England)

The author and his group have devised a method of following the potential spread of tumors by arc-moving beam therapy. Briefly, a metal rod placed on the patient's skin is bent to conform to the expected path of lymphatic spread of a known primary tumor (*e.g.*, a malignant testicular tumor). Such a course or "track" is ordinarily along the axis nodes of the body; in the example given these are the hypogastric, common iliac, and peri-aortic groups in order. Through a series of carefully placed electromechanical devices the arc of a moving beam therapy machine is made to follow such a track and to irradiate only the zones of critical interest. Advantages of such a technic include sparing the total volume of tissue raised to a high dose and perhaps allowing a higher tumor dose with more chance of eliminating the disease because of the smaller volume included in the therapy beam. Details of the device are not given.

Three photographs; 2 diagrams; 3 isodose charts.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

RADIOISOTOPES

The Positron Brain Scanner in the Diagnosis and Localization of Intracranial Lesions. Elliot Rinzler, Wade N. Miller, and Lillian E. Jacobson. J. M. Soc. New Jersey **56:** 243–246, May 1959. (27 South 9th St., Newark, N. J.)

The definition of brain lesions by scintillation scanning for gamma radiations is usually not very precise because of the recording of rays coming into the scanning head at various angles. In an effort to produce more exact localization of brain lesions investigation of positron emitting elements was undertaken. In the typical electron-positron annihilation reaction two gamma-ray photons are released 180° apart. A specialized scanner to detect such reaction has been designed. Two scintillation counters used on opposite sides of the head are connected by special circuitry so that a recording is made only when both counters receive gamma rays simultaneously, as occurs in positron emission and annihilation reaction. The same two opposing counters are then connected to another special circuit, called an anticoincidence circuit, in such a manner that only when one side receives more gamma radiation than the opposite side is a recording made. For these twofold methods of localizing a lesion the term "positrocephalogram" has been used when the positron reaction is detected and "asymmetrogammagram" with use of the anticoincidence circuit. Another step toward better three-dimensional localization is gained by making scanograms not only on each side of the head but also in the anteroposterior axis.

Investigations by others have shown a high degree of localization in some instances. Meningiomas have given the best definition and glioblastomas second best. Deep-seated, small lesions invading the brain stem, ventricle, or sella turcica tend to give poor accuracy, particularly when the tumor is avascular.

An intravenous injection of arsenic 74 (size of dose not stated) is followed in one hour by simultaneous scanning for positron annihilation and asymmetric gamma radiations as described above. Two cases are reported in moderate detail, with reproductions of the resulting scanograms. In the two selected instances localization of subdural fluid collection and parasagittal frontal meningioma are nicely demonstrated.

Two roentgenograms; 1 photograph; 5 scanograms.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

The Lymphatics of the Breast. R. T. Turner-Warwick. Brit. J. Surg. **46:** 574–582, May 1959. (The Middlesex Hospital, London, W. 1, England)

This article is worth reading in full text for physicians engaged in surgery or radiation therapy of the breast. It describes the result of a study of the anatomy of the lymphatics of the breast in 88 patients, with an intravital technic. This consists in the interstitial injection of radioactive gold (Au 198) in the breast. The drainage channels are studied by autoradiography, Geiger counters, or scintillation counters. Some cases were studied by injection of a diffusible dye, such as patent blue.

Briefly the observations made were as follows:

1. The trunk lymphatics of the breast tend to accompany the blood supply.

2. The internal mammary chain is an important pathway of the lymph drainage from both the lateral and the medial halves of the breast.

3. There is no significant drainage of lymph from the breast to contralateral nodes under normal circumstances.

4. The posterior intercostal lymph nodes receive lymph from the breast in a small proportion of patients.

5. The so-called subareolar plexus has not been found to play an important role in the pathway of lymph drainage of the resting breast parenchyma.

6. The minute lymphatics of the deep fascia play no part in the main pathway of the lymphatic drainage of the breast nor in the early spread of carcinoma.

Fourteen autoradiographs; 9 photographs; 5 diagrams.

J. S. ARAJ, M.D.
Toledo, Ohio

The Effects of Varying Amounts of Stable Iodide on the Function of the Human Thyroid. Walter D. Feinberg, David L. Hoffman, and Charles A. Owen, Jr. J. Clin. Endocrinol. **19:** 567–582, May 1959. (Mayo Clinic, Rochester, Minn.)

The aim of this paper is to evaluate an "iodine inhibition test" which is brief and precise. It depends upon the addition of varying amounts of stable iodine to doses of radioiodine.

The authors point out that the hyperthyroid gland is capable of only limited response to the added load whereas the normal functioning gland accepted the additional iodine and in fact was capable of accumulating 10 times the usual amount. This may well suggest that a normal gland functions far below its maximum capacity for handling iodine whereas the hyperthyroid gland is functioning near its capacity.

Four figures; 6 tables. SYDNEY F. THOMAS, M.D.
Palo Alto, Calif.

The Ten-Minute Uptake of I^{131}: A Clinical Study and Comparison with Other Tests of Thyroid Function. H. P. Higgins. J. Clin. Endocrinol. **19:** 557–566, May 1959. (University of Toronto, Toronto, Ont., Canada)

The value of estimating the ten-minute uptake of I^{131} by the thyroid was studied in 333 cases. In hyperthyroidism the deviation from normal values was greater than with the 24-hour uptake. In some mild but definite cases of hyperthyroidism, the ten-minute uptake was clearly abnormal when the 24-hour uptake was normal. The reverse did not occur. In Graves' disease the deviation from normal of the ten-minute uptake was greater than the deviation from normal of the serum protein-bound iodine level, whereas in toxic nodular goiter the degree of elevation above normal of the two values was comparable. Among 221 patients without thyroid disorders, in only 1 was the ten-minute thyroidal uptake of I^{131} above the normal range. One of 33 patients with Graves' disease, and 3 of 20 patients with toxic nodular goiter had ten-minute uptakes in the normal range. The short duration of the test renders it practicable, and allows its adaptation to the use of I^{132}. It does not distinguish iodine deficiency from hyperthyroidism; it is useless in the diagnosis of hypothyroidism, and suffers the slight disadvantage of requiring an intravenous injection. AUTHOR'S ABSTRACT

Treatment of Cancer of the Thyroid Postoperatively with Suppressive Thyroid Medication, Radioactive Iodine, and Thyroid-Stimulating Hormone. B. Catz, D. W. Petit, H. Schwartz, F. Davis, C. McCammon, and P. Starr. Cancer **12:** 371–383, March-April 1959. (Los Angeles County Hospital, Los Angeles, Calif.)

A method of postoperative treatment of thyroid carcinoma is discussed which includes:

(1) Surgical ablation of all accessible thyroid tissue, normal and malignant.
(2) Maintenance of the patient in a euthyroid state (as determined by high normal protein-bound iodine) by means of exogenous medication (2 to 8 grains of desiccated thyroid). This blocks the endogenous production of thyrotropic hormone and thus reduces the steady stimulating effect that TSH may have on cancerous growth.
(3) Periodic administration of exogenous TSH for short periods, followed by tracer doses of 1 to 2 mc of I^{131} to make possible detection, by scanning and scintigram studies, of any functional tissue.
(4) Therapeutic doses of I^{131} (40 to 100 mc) whenever there is evidence of I^{131} localization, to eliminate every potential cancerous cell and remnant of normal thyroid tissue.

A series of 44 patients so treated were followed for two to six years. Twenty-six were considered to be metastasis-free after surgery, 14 of these having had regional lymph nodes which were resectable with the primary tumor. The other 18 had residual metastases in various parts of the body after surgical intervention. The survival rate through the present observation period for the metastasis-free group was 100 per cent.

A lack of correlation was noted between the original histologic diagnosis and the collection of I^{131} by the metastatic tissue. In 78 per cent of the metastatic group there were areas that collected I^{131}. This contradicts statements by others that only a very small percentage will show I^{131} collection based on histologic classification of the excised cancerous tissue. There were 8 deaths in the metastatic group. In 4 of these patients the metastases had ceased to collect I^{131}, and at autopsy a major histologic component at variance with that seen initially at surgery was revealed. This probably represents the natural course of the disease.

It is suggested that thyroid hormone, if given early during the course of the disease in adequately high dosage, will block production of TSH, and thus, with a reduced rate of growth, the tumor will maintain itself as a well differentiated type. This differentiated tissue will then be prepared to respond whenever stimulated with exogenous TSH, promoting collection of I^{131} with destructive effect.

A longer follow-up is necessary to ascertain the value of these promising results.

Four roentgenograms; 6 photomicrographs; 9 scintigrams; 6 tables.

CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

The Use of Radioactive (I^{131}-Labeled) Rose Bengal in the Study of Human Liver Disease: Its Correlation with Liver Function Tests. Carl H. Lum, William J. Marshall, Donald D. Kozoll, and Karl A. Meyer. Ann. Surg. **149:** 353–367, March 1959. (Cook County Hospital, Chicago, Ill.)

With the replacement of the stable iodine atoms of the rose bengal molecule by radioactive iodine (I^{131}), there has been made available a gamma-emitting isotope which can be counted directly over the external surface of the liver and in the blood (Taplin *et al.:* J. Lab. & Clin. Med. **45:** 665, 1955. Abst. in Radiology **66:** 481, 1956.) This isotope has been used in the study of 231 patients: 71 with cirrhosis of the liver, 53 with infectious hepatitis, 23 with calculous obstruction, 36 with carcinoma obstructing the extrahepatic bile ducts, and 48 with normal liver and biliary systems. The diagnosis in the majority of cases was confirmed by either needle liver biopsy, operation, or necropsy, but was accepted in some instances on the basis of unequivocal clinical findings with biochemical confirmation.

Results of the use of radioactive rose bengal in testing liver function and in making a differential study of jaundice indicate that this method is safe, feasible, and practical. Peak radioactivity occurs over the liver within forty-five to ninety minutes after injection, with the highest mean peak level in the normal controls. It was not possible, however, at this time to differentiate hepatitis from stone, in both of which conditions the peaks were in the intermediate range, or cirrhosis from carcinoma, where the lowest levels were seen. Twenty-four hours later such differentiations were possible.

Liver uptake rate (concentration divided by time to attain peak levels) showed a greater difference in the immediate determinations between normal and abnormal conditions; cases of hepatitis and stone could be separated but not cases of cirrhosis and carcinoma. Six and twenty-four hours later, all groups could be easily distinguished.

The blood-level determination of the isotope represents the mirror image of the concentration in the liver or the liver uptake rate.

If the liver uptake rate and blood counts are correlated with certain liver function studies, it appears that both polygonal cell function and the biliary patency of the liver are tested; significant correlations occur more often in total cases than in individual diagnostic groups.

It is most important that *simultaneous* studies of the liver and blood radioactivity levels be made and repeated at the end of twenty-four hours if the test is to have maximum clinical usefulness.

The authors have not been able to use this test as a measure of liver vascularity. In this connection, a technic of preceding the test by radioactive human serum albumin determinations of liver blood volume and circulating blood volume, followed by the rose bengal test, offers a possible method of measuring liver mass *in situ*. A study of this method is now in progress.

Fourteen figures; 7 tables.

Polycythemia Vera. I. Clinical and Laboratory Manifestations. II. Course and Therapy. Paul Calabresi and Ovid O. Meyer. Ann. Int. Med. **50:** 1182–1202; 1203–1216, May 1959. (University Hospitals, Madison 6, Wisc.)

Experiences with 100 cases of polycythemia vera managed with radioactive phosphorus are reported. The first of the two papers deals primarily with clinical

and laboratory manifestations of the disease. Important presenting symptoms include weakness, abdominal pain, thrombotic manifestations, vertigo, erythema, headache, and syncope.

Differential diagnosis between polycythemia vera and secondary polycythemia is frequently difficult, but is important for proper therapy. A helpful point is the normal or slightly reduced arterial oxygen saturation in the presence of increased red cell mass in polycythemia vera. Associated severe respiratory disease may make the clinician think the polycythemia is secondary.

The authors point out a nearly unique symptom described by about one-fourth of their patients: a peculiar form of pruritus aggravated by exposure to heat, especially by bathing in hot water. Prominent physical signs include manifestations of vascular congestion plus hepatosplenomegaly during the hypervolemic phase of the disease. Diseases occasionally associated with polycythemia include peptic ulcer, gout, and occasionally hypernephroma. Possible interrelated causes are discussed briefly.

Typical laboratory findings include hemoglobin values between 16 and 25 grams, hematocrit 55 to 75 per cent, red cell count 6,000,000 to 9,000,000. Multiple other laboratory studies were performed on varying numbers of patients in this series and results are recorded in chart form. About one-fifth of the patients had bone marrow aspiration studies and half of these showed an increase in erythroid elements. It is noted that evidence of panmyelosis may furnish extremely valuable supportive evidence for the diagnosis of polycythemia vera.

The second part of the paper deals with treatment. Phlebotomies should be performed before isotope therapy is undertaken in order to provide more rapid relief of symptoms and to decrease the danger of thrombo-hemorrhagic complications. The effect of isotope therapy becomes manifest only as the destruction of the circulating erythrocytes is not being compensated by the depressed bone marrow.

The average initial dose of P^{32} was 6.0 mc, usually given by mouth. The range was from 2 to 10 mc, dosage being individualized according to body weight and erythrocyte count for each patient. The authors recommend reduction of hypervolemia by a series of phlebotomies, 500 c.c. each, to bring the erythrocyte count below 6,000,000.

The criterion of a successful remission was an erythrocyte count not exceeding 6,000,000 and an absence of symptoms for a period of one year or more. In the 80 cases utilized for follow-up studies, 92 successful remissions were observed in 67 patients. An average oral dose of 7 mc P^{32} was necessary to produce a remission. The average time interval for the occurrence of remission after treatment was five months. About half of the patients in whom a remission was achieved did not require additional or maintenance P^{32}. The other half required approximately 3.4 mc per year maintenance dose. Average duration of remission was three years. Eleven patients in the series reported failed to obtain satisfactory remissions despite an average total dose of P^{32} as high as 33 mc (sic!). The most valuable sign in predicting failure of P^{32} therapy is the presence of marked splenomegaly. If the tip of the spleen projects 10 cm. or more below the costal margin the chances of obtaining remisssion are poor; the larger the spleen the poorer the chances.

Of the 97 patients followed in this study, 28 have died. Six of them (21 per cent) died with chronic granulocytic leukemia. The authors do not feel that this represents an increased rate of leukemia in these patients, particularly when the increased survival times are taken into account. Other prominent causes of death were myocardial infarction (6 cases), and cerebrovascular accident (5 cases).

Data relative to remissions, doses of P^{32}, and other pertinent information are presented in succinct tables and graphs. The average age of onset of the disease was fifty-two years and the median survival eleven years. The only important toxic effect observed from P^{32} therapy was a significant transient depression of peripheral blood elements in 2 individuals, followed in each instance by spontaneous recovery within one month.

The authors are inclined to accept polycythemia vera as one of a group of myeloproliferative disorders, including as other members chronic granulocytic leukemia and myelofibrosis. In conclusion they state "it is particularly important to appreciate that under proper control these patients are entirely capable of leading normal productive lives without physical handicap."

Two graphs; 4 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Treatment of Malignant Edematous Exophthalmos by Implantation of the Pituitary with Yttrium^{90}. Report of Two Cases. G. M. Molinatti, F. Camanni, and A. Pizzini. J. Clin. Endocrinol. **19**: 583–589, May 1959. (University of Turin, Turin, Italy)

Two cases of malignant exophthalmos showed prompt symptomatic improvement following implantation of the pituitary with radioyttrium (Y^{90}), a single pellet (9 mc) in one case and two pellets (18 mc) in the other. The authors believe that this method of treatment combines minimum surgical risk with excellent therapeutic results.

Four figures, including 1 roentgenogram.

SYDNEY F. THOMAS, M.D.
Palo Alto, Calif.

The Use of Small Laboratory Animals in Medical Radiation Biology. VI. Lethal Effect of Co^{60} Gamma Rays in Mice. F. Ellinger, with the assistance of B. F. Lindsley. Naval M. Res. Inst., Res. Rept. 17: 225–232, May 15, 1959. (Bethesda, Md.)

White mice were exposed in specially prepared cages and under controlled geometric factors to doses of cobalt-60 radiation 600 to 900 r in air. The effect of daily injections of 0.5 c.c. of normal saline for five consecutive days beginning on the day of irradiation was also investigated.

Each mouse was observed daily and data were compiled relative to survival and to weight changes. The LD 50–15 days proved to be approximately 800 r (air) and was quite reliably reproducible. Curves demonstrating weight changes in individual groups of mice are reproduced. Animals exposed to the lower doses (600 r air) showed maximum weight depression at the fourth post-irradiation day followed by a slow but constant weight gain. Mice irradiated in the mid-lethal range also showed an early depression of weight followed by a small gain, with a second more pronounced weight loss proceeding either to death or to

later recovery. Animals irradiated at 900 r air lost weight constantly.

The influence of saline injection on the mortality is apparently nil, in that the mice irradiated and then given saline solution showed similar reactions and weight curves in all instances.

The author compares data from this experiment with others he personally has performed. He concludes that cobalt-60 gamma radiation requires for equal biological effect a considerable increase of the radiation dose measured in air over 200 kvp with provision for saturation back-scatter. Compared to the LD 50–15 days of 800 r for Co 60, that for 200-kvp x-rays was 400 r, indicating a "dose ratio" of approximately 2 to 1. Comment is made that the "dose ratio" is different for these two types of radiation for guinea pigs, which are more radiosensitive. Weight curves of mice exposed to the cobalt irradiation did not show a significantly different trend as a group from that observed in mice irradiated with 200-kvp x-rays.

Two photographs; 1 composite weight curve graph; 1 table.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

The Late Effects of Radioactive Strontium on Bone: Histogenesis of Bone Tumors Produced in Rats by High Sr^{89} Dosage. Stanley C. Skoryna and David S. Kahn. Cancer **12**: 306–322, March-April 1959. (McGill University, Montreal, Que., Canada)

The authors studied the late effects on bone of high doses of radioactive strontium, which shares with radium the ability to be deposited in the skeleton and incorporated into the crystalline lattice of bone. The rat was chosen for these experiments, as the growth epiphysis does not close in this species, providing an opportunity to study the effects of deposition of the isotope during relatively active osteogenesis.

Each of 160 rats received six monthly doses, intraperitoneally, of Sr^{89}, having a half life of fifty-two days. The repeated doses were administered with the object of achieving effects similar to those resulting from a single exposure to Sr^{90} with the much longer half life of over nineteen years.

The minimal latent period before the first gross tumor was observed was 188 days. If the 60 animals dying due to the isotope toxicity during the latent period are excluded, a uniform carcinogenic response was seen. Grossly palpable tumors of the long bones or spine developed in 89 animals, while neoplastic changes, often multiple, were found on microscopic examination in all 100 rats living over 188 days.

Microscopic foci of cellular proliferation in the marrow and neoplastic lesions of various sizes were found. It is suggested that the minute foci of proliferating cells represent the earliest stages in the development of tumors. All types of osteogenic sarcoma were observed, with a few showing primarily chondro- or fibrosarcomatous differentiation. This suggests that the factors affecting differentiation of these tumors are not necessarily the same as those inducing them—namely irradiation effects.

In addition to the tumors, the basic changes observed were: (1) disturbance of osteogenesis, (2) fibrosis of the marrow, and (3) cellular proliferation. Changes were maximal in the metaphysis in relation to the epiphyseal cartilage growth, corresponding to the areas of most active osteogenesis.

The histologic changes seen represent the results of several mechanisms: (1) primary effect of irradiation; (2) mechanial weakening of the area secondary to disturbed osteogenesis; (3) physiological remodeling sequences in response to non-specific metaphyseal weakening.

It would seem that the bone-seeking isotopes are most dangerous if the animal is exposed during a period of relatively active osteogenesis, but not rapid turnover. In man, this would appear to be during the final stages of bone growth (*i.e.* puberty) and during the healing stage of fractures.

One roentgenogram; 19 photomicrographs.

CHARLES M. GREENWALD, M.D.
Iowa City, Iowa

RADIATION EFFECTS

The Clinical Radiologist and the Problems of Radiation Hazards. Wendell G. Scott. J.A.M.A. **170**: 421–428, May 23, 1959. (100 N. Euclid Ave., St. Louis 8, Mo.)

This paper assesses objectively the position of mankind today in the environment which has been created by the liberation of radiant energy and power from within the atom. The reports of national and international committees on radiation protection, units and measurements have stimulated lay and medical interest in the subject. Responsibility for the public health aspects has been shouldered by the medical and allied professions.

The growth of diagnostic radiology has contributed enormously to the improved health status and increased human life span during the past fifty years. If diagnostic radiology has produced genetic damage or has had a life-shortening effect, it is not yet apparent.

Among possible somatic ill-effects of radiation, the shortening of life-span has received considerable attention. Numerous studies indicate that sizable total body exposures to radiation accelerate the aging process in animals. However, exposures of a low order and of segmental or partial body distribution do not appear to reduce human life expectancy.

The possibility of irradiation inducing leukemia has been suggested. The number of known cases, however, with antecedent total body irradiation is small. No accurate knowledge of the leukemogenic effect of chronic exposure is available. The threat to patients undergoing occasional diagnostic examinations is very remote indeed; and by workers with ionizing radiations no serious risk is incurred if recommended precautions are observed.

With respect to the genetic effects of radiations, it is known that small doses can increase the mutation rate in hereditary material. Although these mutations are no different from those which have always been occurring in the human race, any increase in mutation rate is undesirable. "No matter what the present average gonadal dose is, it is too high if it can be lowered."

Several things can be done to reduce gonadal exposure. The patient's physician and radiologist should carefully weigh the possible benefits of any diagnostic examination against the possible hazards.

Examinations should be made by competent personnel. Repeat films and nonessential films should be minimized. Fluoroscopy should be limited, especially in children. Equipment should be carefully surveyed for leaks, obsolescence, etc. In making radiographs, the use of adequate aluminum filtration in x-ray tubes, maximum practicable target-skin distance during exposures, careful beam collimation, high-speed films and screens, gonad-shielding devices when indicated, and the use of image-intensifiers, all will reduce the quantity and improve the quality of the x-ray beam.

A plea is entered for a calm, mature attitude toward the nuclear era, and for an end to the confusion between the hazards of diagnostic radiology and those of thermonuclear warfare.

Every physician must exert himself to keep gonadal radiation doses at a minimum; and must recognize that the key to safe use and control of medical radiation lies in the proper education of its users in the fundamentals of radiology, radiobiology and genetics.

Four roentgenograms; 4 photographs; 2 tables.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

Leukemia and Medical Radiation. Donald W. Polhemus and Richard Koch. Pediatrics **23:** 453–461, March 1959. (D. W. P., 644 North Central Ave., Glendale 3, Calif.)

The medical radiation histories of 251 leukemic children, seen at the Childrens Hospital of Los Angeles between January 1950 and July 1957, were compiled and compared with those of a group of healthy children. In general, exposure to radiation was significantly more frequent among the leukemic group.

Thymic irradiation was found to be associated with six times the usual incidence of leukemia, the data being highly significant ($p < 0.01$). Statistical analysis of the data relative to fluoroscopic studies of the heart or gastrointestinal tract, even though not highly significant, does indicate the possibility of a relationship between this type of radiation and an increased incidence of leukemia ($p < 0.05$). Diagnostic roentgenography had been performed more frequently in the leukemic group, but the level of significance was not great ($p < 0.05$).

Maternal exposure to roentgen rays during pregnancy had occurred somewhat more commonly in the leukemic group, but the difference was too small to be significant ($p < 0.10$).

Six tables.

In a Letter to the Editor (Pediatrics **23:** 1200, 1959), Dr. Robert W. Miller, of San Francisco, questions some of the methods employed in the above investigation and the conclusions drawn: (1) If the children in the two groups were not of similar socioeconomic status, unequal access to medical care could explain the differences in the frequency of a history of radiation exposure. (2) If different methods of contact were employed for the two groups, this could contribute to a difference in the results obtained. (3) Much of the difference in the history of radiation exposure came from leukemic children given thymic irradiation earlier in childhood. Attention is called to the possibility that thymic enlargement itself may signify a predisposition to leukemia. (4) The subtle changes in physiology occurring well before leukemia can be diagnosed could conceivably increase susceptibility to infection or produce ill-defined symptoms for which radiologic procedures would be performed. In this event leukemia would predispose to irradiation, rather than the converse. In a reply, Dr. Polhemus supplies additional information to clarify some of these points.

Eight Further Cases of Radiation-Induced Cancer. Michael Garrett. Brit. M. J. **1:** 1329–1331, May 23, 1959. (Radium Institute, Liverpool, England)

Carcinoma induced by radium or x-ray was at first seen only in radiation workers, but in recent years most cases have occurred in patients receiving radiotherapy for malignant or, more often, benign conditions, especially protracted multiple exposures to young developing tissue. Among the benign conditions for which radiation has been employed are thyrotoxicosis, hemangiomata, psoriasis, pruritus, and lupus vulgaris.

Radiation-induced carcinoma most commonly occurs in the skin, but has been reported also in bone, the mediastinum, thyroid, stomach, pharynx and larynx, and tongue. Most growths are squamous-cell carcinoma, but there are records of osteogenic sarcoma, fibrosarcoma, and basal-cell carcinoma. The latent interval between radiation exposure and carcinoma has varied from two to forty-nine years.

Eight case histories of radiation-induced laryngeal and pharyngeal carcinoma are presented here, including a carcinoma of the vocal cord, bringing to 6 the number of true laryngeal carcinomas assumed to be radiation-induced. All 8 patients were originally treated for thyrotoxicosis.

One photograph.

GORDON L. BARTEK, M.D.
Grand Rapids, Mich.

Postirradiation Malignancies of the Pelvic Organs. Edmund R. Novak and J. Donald Woodruff. Am. J. Obst. & Gynec. **77:** 667–675, March 1959. (The Johns Hopkins Hospital, Baltimore, Md.)

The authors discuss the question of malignant neoplasms arising after irradiation of the pelvic organs, based on their experience at the Johns Hopkins Hospital. The investigation covered patients treated for cancer of the cervix by combinations of radium and x-ray therapy. The amount of radium generally used was 4,800 mg. hr., given in two twenty-four-hour doses, each dose consisting of 50 mg. in a plaque to the cervix and an additional 50 mg. in a tube to the endocervical canal. The radium applications were at two-week intervals, after which deep x-ray therapy was given to tolerance, 10,000–17,000 r, measured in air, through four portals, with either a 200- or 400-kv. machine. Patients were not included in whom menopause was induced by irradiation for a benign condition.

Three cases of endometrial adenocarcinoma developing postirradiation are reported in detail. In all 3, the original histologic diagnosis was epidermoid carcinoma. The first 2 showed a time lag of eight and six years, respectively, between the irradiation and the development of the new tumor. It is noteworthy that these 2 patients showed a recurrence of the original epidermoid tumor shortly after treatment for the new cancer. This seems to verify what has been accepted as one of the main effects of radiation, the tendency to enmesh and fibrose nests of viable tumor cells so that a more general dissemination occurs. The third case is considered highly unusual. A Papanicolaou

smear was positive for cancer although there was no overt cervical lesion. Biopsy showed an epidermoid cancer. The patient received radium and a full course of deep x-ray therapy, which was completed in February 1954. In March 1955, she complained of vague abdominal discomfort. X-ray examination revealed a duodenal ulcer, and this was thought to be responsible for the symptoms. Dilatation and curettage were performed, however; the few fragments of endometrium and specimens of cervix consisted only of atrophic tissue. Six months later the patient had vaginal bleeding. Curettage disclosed an extensive adenocarcinoma. A bilateral salpingo-oophorectomy was performed; one lymph node was removed for study, but the process was too extensive for even a radical Wertheim procedure. Histologic examination showed adenocarcinoma throughout the myometrium with involvement of both serosal surfaces and endometrium. Nowhere was there any evidence of the original epidermoid tumor. The short interval between irradiation and the second cancer makes any causative relationship seem improbable if not impossible. Whether irradiation might cause malignant change in a previously present benign lesion, such as adenomyosis, seems highly unlikely in view of the frequency with which such uteri are subjected to irradiation.

A significant number of women who received the usual cancerocidal dosage of radium and deep x-ray therapy for cervical carcinoma were found at a later date to have an early epidermoid lesion in the vagina, although the cervix itself was completely healed. That this was a new lesion rather than recurrence or metastasis is suggested by the intraepithelial pattern of the vaginal growth as compared to the markedly anaplastic infiltrative appearance of the original cervical tumor. The new tumor was generally in the region of the fornices or upper vagina; in other words, in relation to the site of initial irradiation, the lower tract tumor was at about the same distance below as the endometrial lesion might be situated above the primary target area.

Similarly there has been a tendency to a disproportionate incidence of vulvar cancer years after the completion of radiotherapy to the cervix. Again, the tumor is epidermoid like the initial cervical tumor, but the intraepithelial nature of the second tumor is so totally different as to indicate that the vulvar lesion is not a late manifestation of the primary tumor.

Only 2 cases were seen in which an ovarian cancer occurred long after irradiation. When large amounts of x-irradiation are utilized, it seems probable that the ovary is in greater proximity to points A and B than the lower tract or fundus. Thus, it could receive sufficient radiation dosage to prevent any carcinogenic stimulus, rather than receiving subthreshold radiation which might serve as an actual causative factor in the evolution of later cancer.

Although admittedly there are a great many inadequacies in our knowledge of the mode of action and sequelae of radiotherapy, the authors feel strongly that this does not imply that its use should be abandoned or curtailed. Because of the possibility that there may be some causal relationship between its use and the later development of other forms of genital neoplasm, it is paramount that the gynecologist does not lose sight of this possibility and continues to follow irradiated patients with circumspection.

Five photomicrographs.

Certain Structural Aspects of Lymphocytes and Monocytes in Relation to the Clinical Condition of Persons Exposed to Ionizing Radiation. D. O. Shiels. Brit. J. Radiol. **32**: 306–314, May 1959. (Hawthorn, Victoria, Australia)

This paper presents an original investigation of the blood cells designed to discover some early and reliable changes in the blood picture which would be indicative of damage due to ionizing radiation. The author has studied the ratio of large to small lymphocytes L/S, the ratio of monocytes plus large lymphocytes to small lymphocytes L + M/S, the percentage of lymphocytes which show granules in the cytoplasm, and the percentage of the monocytes which are of a particular type, in persons exposed to radiation. From these factors, certain indices have been derived which have shown more clear-cut distinctions between different groups of persons examined than did the factors themselves. Index (1) is the percentage of the lymphocytes which have granules in the cytoplasm divided by the ratio L + M/S. Index (2) is the resultant value divided by the percentage of the monocytes designated as being of the "B" type. The authors report the results of the investigation in 7 subjects who in their daily work are exposed or could be exposed to radiation.

The results of these studies show a definite difference in the factors and indices mentioned for persons exposed to radiation when unwell and when well. The value of this new test is important as a useful indication in assessing the response to exposure and certainly much more sensitive and consistent than any of the usual blood tests.

Seven tables.

J. S. ARAJ, M.D.
Toledo, Ohio

The Hierarchy of Modes of Radiation Death in Specifically Protected Mice. Henry Quastler and Marion Zucker. Radiation Res. **10**: 402–409, April 1959. (Brookhaven National Laboratory, Upton, N. Y.)

There are several modes of acute radiation death. Which of them occurs in a particular instance depends on the quantity and quality of radiation used, the species of animal, the parts which are irradiated or shielded, concomitant treatments, and a number of other factors which are not controllable or, at least, not controlled. In mice and rats, the mode of death which is the earliest to occur after the smallest lethal dose (about 600 rads to the whole body) is called "marrow death"; it is associated with aplasia of the hemopoietic tissues and can be prevented by providing some normal hemopoietic tissue, either by partial shielding or by transplantation. Animals so protected tolerate doses up to about 1,200 rads; with doses above this, death occurs from intestinal damage before hemopoietic recovery can begin. Intestinal death is due to a radiation response of the small bowel and can be prevented by shielding most of the small bowel or by parenteral administration of fluids and electrolytes. Mice specifically protected against both marrow and intestinal death will survive still higher doses until another system is so severely impaired that the animal succumbs. An investigation employing specific protection is described.

Marrow Syndrome: Hemopoietic recovery after irradiation with 3,000 rads was studied histologically in animals in which both hind legs, the lower jaw, and as much of the intestine as could be exteriorized was shielded. These studies in animals protected against lethal intestinal damage show that hemopoietic recovery

can proceed normally even in animals which have been heavily irradiated and are fatally damaged.

Intestinal Syndrome: The LD 50 (intestinal) for acute intestinal death (in three and a half to four and a half days) is about 1,200 rads. Death from intestinal damage does not occur, as a rule, with doses up to 6,000 rads (possibly more) if the exteriorized intestine is shielded during irradiation. In the authors' experiments the duodenum was unprotected. Denudation of the duodenum is compatible with survival; regeneration occurs even after doses of several kilorads.

Oral Death: The LD 50 (oral) was about 1,700 rads. No oral death occurred in mice in which the lower jaw had been shielded by wrapping in lead foil.

Death in Mice Protected against Marrow, Intestinal, and Oral Syndrome: Mice irradiated with several kilorads, even though protected against marrow, intestinal, and oral death, succumbed to an unidentified disturbance.

Two figures; 3 tables.

The Effect of Pitressin on Postirradiation Polydipsia and Polyuria in the Rat. Clyde M. Williams and George M. Krise. Radiation Res. **10:** 410–417, April 1959. (C. M. W., Radioisotope Unit, VA Hospital, Pittsburgh 40, Penna.)

The effect of the antidiuretic hormone vasopressin (Pitressin) on postirradiation thirst and diuresis in the rat was studied. It was found that 500 mU of Pitressin tannate in peanut oil, injected intramuscularly immediately before or immediately after whole-body irradiation by 1,500 r of Co^{60} γ- rays, inhibited polydipsia and polyuria in the adult rat. Aqueous solutions of Pitressin, when injected intramuscularly either before or after irradiation, did not inhibit the polydipsia and polyuria evoked by 1,500 r of whole-body irradiation.

Rats deprived of water for the first twenty-four hours after 500 r of whole-body irradiation did not excrete urine in amounts significantly greater than were excreted by nonirradiated controls.

Water intake and urine output during the first twenty-four hours after 1,500 r of whole-body irradiation decreased linearly with increasing dose of injected Pitressin tannate in peanut oil; 150 mU was found to be the minimum dose of Pitressin which produced a water intake and urine output not significantly different from those of the nonirradiated controls during the first twenty-four hours postirradiation.

The irradiation of Pitressin tannate in peanut oil (in a concentration of 1,500 mU/ml) by doses up to 20,000 r did not alter the ability of Pitressin to inhibit the polydipsia and polyuria evoked by 1,500 r of whole-body irradiation.

One graph; 6 tables.

Effect of X-Radiation on DNA Metabolism in Various Tissues of the Rat. I. Incorporation of C^{14}-Thymidine into DNA during the First 24 Hours Postirradiation. Oddvar F. Nygaard and Richard L. Potter. Radiation Res. **10:** 462–476, April 1959. (University of Michigan Medical School, Ann Arbor, Mich.)

The effect of total-body x-irradiation on the deoxyribonucleic acid (DNA) synthesis in thymus, spleen, and small intestine of the rat was studied throughout the first twenty-four hours after exposure to doses ranging from 50 to 800 r. The amounts of radioactivity from thymidine-2-C^{14}, incorporated into DNA over one-hour periods were used as a relative measure of synthesis.

A rapid and extensive decrease in the incorporation of radioactivity was observed in all three tissues after the highest doses, with a gradually decreasing effect with lowering of dose. In thymus and spleen there was no indication of recovery within the twenty-four-hour period, whereas in the intestine there was an increase in labeling after eight hours at all dose levels.

The data obtained for the small intestine are compatible with the assumption that the decreased incorporation is, in part, caused by a delayed onset of DNA synthesis in some of the cells. This delay, at least at the earliest times after irradiation, is not the result of inhibition of mitosis.

Seven graphs.

The Relative Biological Effectiveness of 200-Kvp X-Rays, Cobalt-60 Gamma-Rays, and 22-Mevp X-Rays, Determined from the Dose-Survival Curve of *Saccharomyces cerevisiae*. W. K. Sinclair, S. E. Gunter, and A. Cole. Radiation Res. **10:** 418–432, April 1959. (W. K. S., M. D. Anderson Hospital and Tumor Institute, Houston, Texas)

The relative biological effectiveness (RBE) of cobalt-60 γ-rays (1.17,, 1.33 Mev) and 22-Mevp x-rays from a betatron with reference to 200-kvp x-rays (primary h.v.l. 1.4 mm. Cu) was determined by using the slope of the survival curve of the yeast *Saccharomyces cerevisiae* (based on macrocolony counts) as the biological end point. The average RBE of five experiments was found to be 0.85 for cobalt-60 γ-radiation and 0.85 for 22-Mevp x-radiation, with uncertainties of the order of ± 0.05 in each case. No significant difference between cobalt-60 γ-radiation and 22-Mevp x-radiation was demonstrated.

Ten illustrations; 5 tables.

A Chronic Irradiation Source for Small Animals. Howard E. Noyes. Radiation Res. **10:** 400–401, April 1959. (Walter Reed Army Institute of Research, Washington, D. C.)

A simple chamber for chronic irradiation of small animals is described. This consists of two pieces of double-thickness glass embedded in 7.0 mm. of lead with an air space of 2 mm. between them. The two pieces of glass are sealed in position with hypoxy resin. A cover of 7.0 mm. of lead (supported by aluminum to provide rigidity) is employed to reduce irradiation when the chamber is not in use. The chamber is filled with an isotope solution (cesium 134). A wooden frame supports a stainless steel pan, which will house 60 mice or 15 to 20 rats or guinea-pigs. Food and water are provided to last one week, so that the investigator need go into the irradiation area only once a week. Exposure to irradiation under these conditions need not exceed 10 to 20 seconds per week. The radiation dose can be varied by inserting sheets of lead between the glass and the pan or by raising the pan. When a dose of 100 mr is placed in the chamber and a sheet of lead 7.0 mm thick is placed between the chamber and the pan, the mice at the bottom of the pan receive 25 r equivalent per day.

One drawing.